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EARLY FIRST TRIMESTER FETAL GROWTH RESTRICTION AND ITS CORRELATION WITH ADVERSE PREGNANCY OUTCOME

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ABBREVIATIONS

- FGR – Fetal growth restriction
- TVS – Transvaginal Sonography
- GS – Gestational Sac
- YS – Yolk sac
- CRL – Crown-rump length
- SGA - Small for Gestational Age
- HR – Heart rate
- LMP – Last menstrual period
- POG - Period of Gestation
- EDD - Expected Date of Delivery
- P/A - Per Abdomen
- P/S - Per Speculum
- P/V - Per Vaginum
- USG - Ultrasound

INDEX

S.No.	TITLE	PAGE NUMBERS
1.	INTRODUCTION	1
2.	AIMS AND OBJECTIVES	3
3.	REVIEW OF LITERATURE	4
4.	MATERIALS AND METHODS	24
5	OBSERVATIONS AND RESULTS	27
6	DISCUSSION	48
7	SUMMARY	53
8	CONCLUSION	57
9	BIBLIOGRAPHY	57
10	ANNEXURES ANNEXURE I ANNEXURE II ANNEXURE III	64-72
11	Master chart outline	73

"EARLY FIRST TRIMESTER FETAL GROWTH RESTRICTION AND ITS CORRELATION WITH ADVERSE PREGNANCY OUTCOMES"

INTRODUCTION

Fetal growth restriction (FRG) can be described as a condition where fetus fails to attain its genetically set on growth potential. Restricted fetal growth is a major pregnancy complication and it also determines prenatal morbidity and mortality. Increasing evidence suggests that Fetal growth restriction (FGR) might have origins in early pregnancy. Early onset FGR has a strong association with adverse neonatal outcomes, while late-onset FGR presents with subtle biophysical abnormalities and is therefore more difficult to diagnose[1].

Early recognition of fetuses at risk of Fetal growth restriction (FGR) enables more appropriate surveillance and management, which has been shown to reduce risks of adverse fetal outcomes. To study early fetal growth restriction, it is preferable to use ultrasonographic imaging with estimation of change over specific time intervals as it has the ability to diagnose early pregnancy growth restriction and related conditions. Serologic markers are not specific and show signs only after loss of pregnancy were diagnosed[2].

Transvaginal ultrasound (TVUS) is by and large used to make diagnosis of intrauterine pregnancy and developmental follow-up due to its capability to produce high-resolution images, low inter-observer variability with high reliability. Parameters like Crown-rump length (CRL), Gestational sac diameter (GS), fetal heart rate (HR) and yolk sac (YS) are measured to diagnose early pregnancy. Any deviations in the parameters shown above during ultrasound are further investigated to predict any possibility of first trimester pregnancy loss [1,2, 3].

Ultrasound findings associated with subsequent miscarriage include a slow embryonic heart rate (HR), less than normal gestational sac diameter (GS) and abnormal yolk sac diameter. Smaller Crown-rump length (CRL) findings have also been associated with subsequent adverse pregnancy outcomes. Chromosomal defects not only have a high intrauterine lethality

rate but can also be associated with fetal growth restriction like smaller Crown-rump length (CRL) in the first trimester of pregnancy which further leads to miscarriage[3].

Deviation from normal parameters can be identified by plotting the measurements on fetal growth charts. It has been observed that these practices are effective in preventing adverse outcomes[4]. Most obstetricians and sonographers in developing countries follow fetal growth charts generated through studies on western populations with different socioeconomic and nutritional status from those of their own countries. Nevertheless, studies of World Health Organization (WHO) and INTERGROWTH-21st century have developed multiethnic international fetal growth charts to overthrow the constraints of existing reference charts for universal practices. Other studies in further years have also confirmed the effectiveness of these charts in identifying deviations. However, the effectiveness and suitability for settings such as the Indian setting should be assessed; use of the WHO chart should be adjusted to the local context [5, 6.] The study aims to evaluate the prognosis of pregnancies which have early first trimester fetal growth restriction. By learning of any abnormalities and their subsequent outcomes, the prospective parents can be counseled and advised. Earlier risk assessment will help in better management of broader health problems.

AIMS AND OBJECTIVES

The aim of the study "**Early first trimester fetal growth restriction and its correlation to adverse pregnancy outcome"** is **–**

1. To evaluate the earliest and most reliable parameter of fetal growth restriction on ultrasound.

2. To determine the degree of correlation between early first trimester ultrasound findings and adverse pregnancy outcome.

REVIEW OF LITERATURE

The miscarriage of an early pregnancy is amongst one of the most prevalent medical complications in humans. It has been observed that approximately 50% of conceptions eventually at the end of first trimester have a bad outcome. Most miscarriages occur within the first month after the preceding menstrual period, so that the patient is often unaware of both the conception and the subsequent abortions. Former studies have reported pregnancies which had significantly small CRL than expected later on had higher chances of ending up in miscarriage[2, 3].

Etiology

The etiology can be clinically divided into three factors clinically that is, fetal factor, maternal factor and placental factor. Howsoever, overlapping has been seen in all three pathogenesis[7].

Fetal factor: Genetic abnormalities in fetus have been seen in 5% percent to 20% percent of cases of fetal growth restriction. The following genetic cause can be there such as aneuploidy, single-gene mutations, uniparental disomy partial deletions or duplications, ring chromosome, and aberrant genomic imprinting. Amongst them most commonly aneuploidy is the cause for fetal growth restriction before 20 weeks. Fetal infection is causes in 5%-10% of cases, cytomegalovirus and toxoplasmosis being the most common amongst them. Other infectious agent may be varicella-zoster virus, malaria, syphilis, and herpes simplex. Other causes may be non chromosomal congenital anomalies or other specific syndromes[8, 9].

Maternal causes: Maternal disorders can adversely interfere with uteroplacental – fetal blood flow. These conditions are chronic hypertensive disease, gestational diabetes mellitus or pregestational diabetes mellitus, autoimmune disease like antiphospholipid syndrome, systemic lupus erythematosus, severe cardiopulmonary or renal diseases, sickle cell disease, severe anemia and malnourishment, substance abuse like excessive use of alcohol, addiction to recreational drugs like cocaine, nicotine, heroin, marijuana, etc, anti-neoplastic drugs or exposure to radiation, chronic ante partum hemorrhage, less than normal pre-pregnancy

weight or poor weight gain during the gestation higher end of maternal age, very less inter pregnancy interval, high altitude residency, multiple pregnancy, malformations in uterine structure and any assisted conception. If pregnant mother is herself malnourished and is with restricted growth then there is twice as much risk of giving birth to fetal growth restricted fetus. Mother's nutritional status is also responsible for development of fetus, which may end up being 10% of FGR fetus[8, 9].

Placental cause: Chromosomal placental mosaicism (CPM), presenting with placental trisomy and a chromosomally well developed fetus, is identified in 33% of FGR with placental infarction, decidual vasculopathy and 10% of idiopathic cases of FGR. Placental abnormalities like bilobate or circumvallate placenta, small sized placenta, any placental mesenchymal dysplasia, anomalies related to umbilical cord like single artery, velamentous or marginal cord insertion are some of the other causes of fetal growth restriction. History of any maternal morbidity has negative impact on the fetal growth via affecting its placental functions[8, 9].

The Early First Trimester Scan

The earliest sign of pregnancy is persistence of vascularised corpus luteum beyond day 28. This appears as a cystic, hyper echoic, isoechoic or echogenic area in active ovary and intense peripheral blood flow signals on color flow mapping. Implantation commences on day 19 of the cycle and is completed by day 23. Conceptus at this stage is 0.1mm in length but cannot be seen with currently available ultrasound equipment. Gestational sac diameter gets visualized between 4 weeks plus 1 day to 4 weeks plus 3 day by TVS scan. Gestational sac perhaps could be demonstrated at as early as beta HCG of 300 MIU/ml but it is evident by discriminatory level of 1000 MIU/ml. Failure to demonstrate gestational sac at this level might indicate failed intrauterine pregnancy or ectopic pregnancy. Gestational sac may be round or oval and the calculation of its quantification is done by mean sac diameter. Gestational sacs are first seen when they reach a size of 2-3 mm. As MSD reaches to 10mm, a double decidual sign appears. First structure to appear within GS is yolk sac; with TVS yolk sac can be first visualized by MSD 5 mm and evident by MSD 8 mm. The maximum diameter of a healthy yolk sac is 5-6 mm, which can be used to calculate gestational age. Irregular or abnormal yolk sac size or morphology needs serial evaluation to follow the outcome[8].

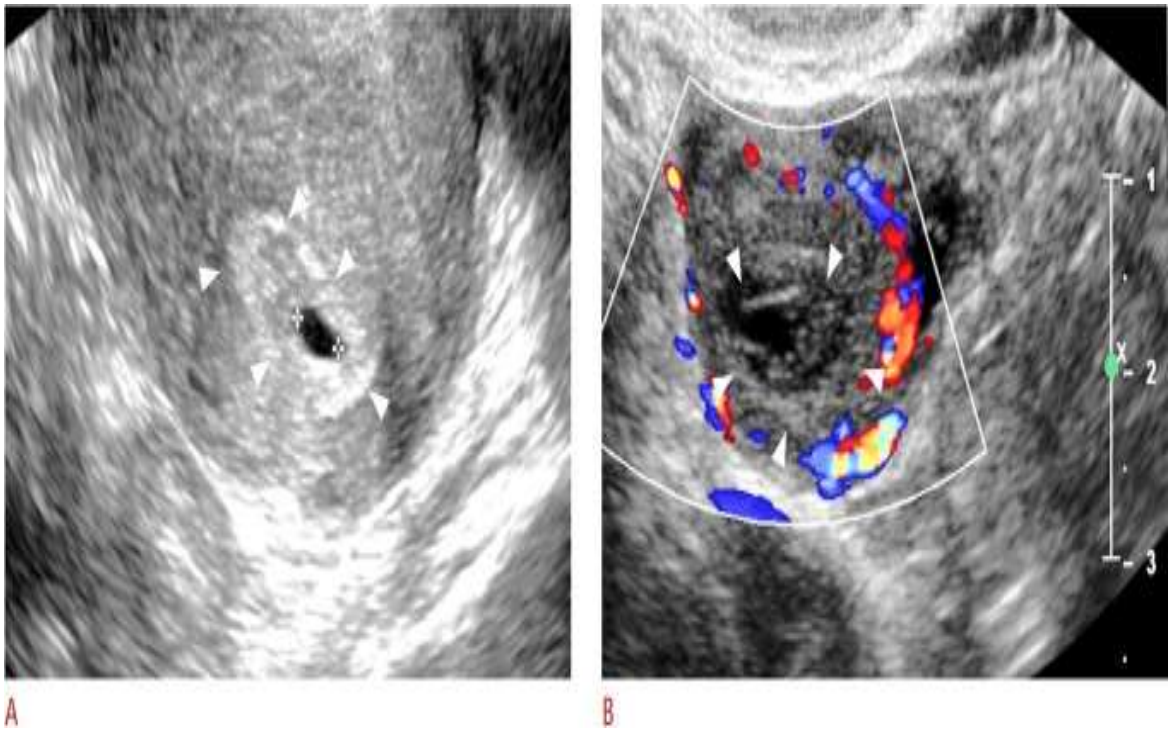

Figure 1 A. Transvaginal ultrasonography (TVUS) reveals an anechoic structure in company of peripheral echogenic tissue (arrowheads) representing a gestational sac in the uterine cavity of a pregnant female with positive urine pregnancy test report. B. TVUS shows a circumscribed heterogeneous structure with peripheral vascularity in the right ovary compatible with a corpus luteum

Embryonic cardiac activity appears at 34 days of gestational age, embryo length is 1.6 mm, embryonic heart rate is about 100-115 bpm and slowly progresses to 144-159 bpm by week 8. From week 8-10, the embryo and amniotic membrane growth takes place at a pace of 1 mm per day. Fetal length at this stage is equal to amniotic sac diameter. 12 mm of embryonic length corresponds to 12 mm of MSD. The brain and trunk start to become distant by 8-9 weeks of gestation. Embryonic movements become apparent at the ending of the 8 weeks of gestation. Developing embryos can be measured end to end to assess the gestational age, this is known as crown rump length. The distance from top of head to bottom of rump of embryo in neutral posture and there should not be any flexion or extension. Three readings are taken then their mean is calculated. This is used to calculate the gestational age from 5 weeks 3 days till 13 weeks 6 days. In pregnancy this is the most trusted parameter to measure gestational age. Ultrasound is the well founded tool to evaluate early complications in pregnancy [7, 8, 9].

Criteria for failure of pregnancy include embryos without pulse which are 7 mm or more in CRL or a gestational sac diameter of larger than 25 mm with no embryo. Prognosis is poor if we find embryonic bradycardia suboptimal embryonic growth and unusually large or small gestational sac, an abnormal yolk sac, a hemorrhagic chorionic sac or amniotic cavity same as diffuse or focal variability echoic specks and a thin trophoblast, chorio residual and amnio residual separation are seen in pregnancy with pain or bleeding but at times also asymptomatic. So objective evaluation is done which includes volume assessment and assessment of the sac perimeter. It is important for serial comparison.

Assessment of gestational age:

To assess growth restriction, it is important to have a proper evaluation of gestational age. Crown rump length measurements between ages 8 to 14 weeks provide the most accurate assessment of fetal age. This equals the accuracy of assessment of ovulation studies[1] and embryo transfer calculations[8,9]. Mean gestational sac diameter which is measured before embryo is visualized has accuracy of $\pm 5\ days$.

Table 1

Timeline of normal fetal development

Time (wk)	**Development milestone**
4.5-5	Appearance of gestational sac
5-5.5	Yolk sac becomes apparent
6	Embryo is seen, cardiac pulsation
6.7-7	Amniotic membrane appears
7-8	Appearance of fetal spine
8	Head and limbs begin to appear as distinct from torso
8-8.5	Fetal motion is appreciable
8-10	Rhomb encephalon appears

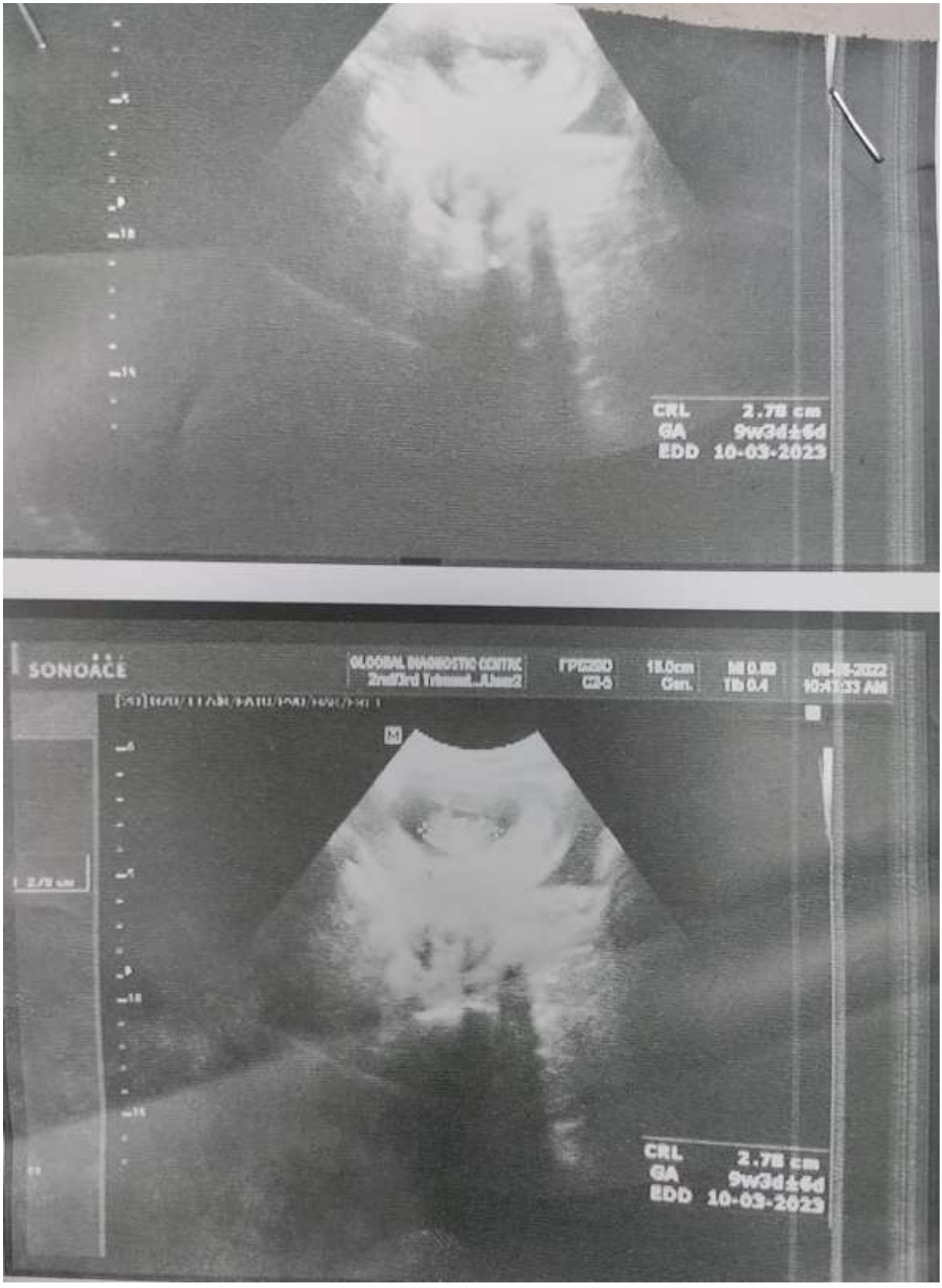
CRL 2.78 cm
GA 9w3d±6d
EDD 10-03-2023
SONOACE
CRL 2.78 cm
GA 9w3d±6d
EDD 10-03-2023

Figure 2

Table 2

Findings diagnostic of and suspicious for pregnancy failure

Finding	Diagnostic of pregnancy failure	Suspicious for pregnancy failure
Absent fetal cardiac activity by the time CRL is a certain size	CRL ≥7 mm	CRL <7 mm
Absent embryo by the time the gestational sac is a certain size	MSD ≥25 mm	MSD 16-24 mm
Absent embryo in two consecutive exams separated by time	Nonvisualization of an embryo with fetal heart rate 2 wk after identification of gestational sac without yolk sac	Nonvisualization of an embryo with fetal heart rate 7-10 days after US showed gestational sac with yolk sac
	Nonvisualization of an embryo with fetal heart rate 11 or more days after identification of a gestational sac with yolk sac	Nonvisualization of embryo 6 wk after LMP
Abnormal morphology of the gestational sac, amnion, and yolk sac	-	Amnion seen adjacent to yolk sac with no visible embryo (empty amnion)
	-	Yolk sac >7 mm
	-	Disproportionately small gestational sac (in relation to size of embryo, <5 mm difference in size between MSD and CRL)

HUGH P. ROBINSON (1973)[10] studied ultrasound Measurements of the Fetal Crown Rump Length as mode of estimating maturity in first trimester of pregnancy stated that no other procedure allows such a degree of accuracy and reliability at this or any other stage of pregnancy, and it is now becoming our practice whenever possible to estimate in this way the maturity of "at risk" pregnancies and those where the history about menstrual cycle is not clear.

J S Oh et al (2002)[11] conducted a study in year 2002 to determine the gestational sac diameter (GSD) in pregnancies between first 4 to 6 weeks of pregnancy by using transvaginal sonographic measurement. This was done by calculation of dates from the preceding menstrual period. It can predict whether a pregnancy will result in a normal term birth or in any spontaneous miscarriage. They have found that there was no difference in the gestational sac diameter measurement at 28-35 days of gestation since the last menstrual period either in normal and abnormal pregnancies. However, they concluded that less than expected sac diameter measurement in the pregnancy at gestational age between 5-6 weeks from the last menstrual period has a predictive factor for subsequent miscarriage.

E Jauniaux et al (2005)[12] did a study to see the use of ultrasonography imaging in management by diagnosing and investigating early pregnancy failure, they investigated both singly and in combination in attempts to predict those pregnancies that will result in miscarriage. Ultrasound variable combined with maternal serum hormonal levels, maternal age, history of smoking habits, any bad obstetric history and the presence of vaginal bleeding have all been combined in multivariate analyses, with mixed results. Ultimately, the fact remains that the vast majority of early pregnancies in which the viability or likely outcome of the pregnancy are uncertain will require careful counseling and timely follow-up, with limited use in clinical practice of a 'chance of a successful outcome'. Such predictors will, however, provide health care professionals with a tool with which to determine the timing of such follow-up and enable more appropriate counseling with regard to possible short- and long-term outcomes.

T Y leung et al(2008)[13] studied the factors first trimester that could affect final birth weight and they found that smaller than expected crown rump length, maternal serum levels of pregnancy-associated plasma protein A and free beta-human chorionic gonadotropin when found in lower level were the risk factors. Their data showed lower PAPP-A and smaller CRL are the individual elements that influence the final birth weight, hence the risk of the fetus being SGA is increased.

Verburg et al (2008)[14] have studied charts for dating of pregnancy by ultrasound and reference curves that are used for fetal biometry were further presented. Better prediction of the accurate date of delivery can be done by early ultrasound examination, up to 24 weeks of

pregnancy, rather than using last menstrual period for dating and calculation. If earlier ultrasound assessment is done in pregnancy, preferably between 10 and 12 weeks of gestation, the better the estimate of gestational age.

Table 3

Crown-rump length (CRL) measurements in relation to gestational age for the original equation fit reported by Verburg et al.[2]compared to our model fit of the simulated data			
	Verburg's original reported equation	Equation from the simulated data	
CRL (mm)	Median GA (Weeks) predicted from CRL	Median GA (Weeks) predicted from CRL	Difference in GA (days)
5	6.336	6.324	0.082
10	7.503	7.497	0.041
15	8.312	8.31	0.015
20	8.962	8.962	-0.003
25	9.519	9.521	-0.017
30	10.015	10.019	-0.026
35	10.469	10.474	-0.032
40	10.892	10.897	-0.035
45	11.29	11.296	-0.036
50	11.67	11.675	-0.036
55	12.034	12.039	-0.033
60	12.386	12.39	-0.029
65	12.727	12.731	-0.023
70	13.06	13.063	-0.016
75	13.386	13.387	-0.008
80	13.706	13.706	0.001
85	14.021	14.019	0.012
90	14.331	14.328	0.023
95	14.638	14.633	0.036
100	14.942	14.935	0.05

Mukri F, Bourne T, Bottomley C, Schoeb C, Kirk E, Papageorghiou A (2008) [15] - examined that whether viable early pregnancies which later on ended in miscarriages had exhibited any corroboration of early first trimester fetal growth restriction and they also studied that if there was any deviation present between the observed crown-rump length and expected crown-rump length from gestational age 5 weeks till 10 weeks then followed them for viability at 11-14 weeks reported that Early First trimester growth restriction detected with certain LMP and CRL for gestation was smaller is subsequently ended in intrauterine death.

C bottomley et al(2009)[16] in their study they had concluded that viability or non-viability of pregnancy can be confirmed by its observing the gestational age of pregnancy at that time as it is significantly correlated to it. In an asymptomatic woman having no history of any prior ectopic pregnancy, TVS can be delayed until 49 days. There data had suggested that this could reduce the number of unnecessary inconclusive scans, without any associated increase in risk of morbidity from missed ectopic pregnancies.

Reem hasan et al (2009)[17] did studies on 4510 women to see the association first trimester bleeding pv and miscarriage they found that vaginal bleeding is a common, and potentially alarming, symptom in early pregnancy. They found that in cases of intrauterine pregnancies though light bleeding or spotting for a short duration of time does not increase risk of miscarriage but painful bleeding episodes with heavy flow similar to or greater than usual menses were associated with a higher risk of miscarriage. It is pertinent to note here that though only 2% women in their study reported heavy bleeding but episodes demands greater concern for the health of a pregnancy.

These above studies suggest that evaluation in early first trimester of pregnancy is important as there is correlation between discordance of growth and later on ending up with pregnancy loss. Therefore to improve maternal well being it is important to identify risk factors and detect abnormality at the earliest so that there is earliest management. This will have lesser physical and mental burden to the parents and overall improvement on maternal healthcare.

Mook-Kanamori et al (2010)[18] found that the maternal physical features and lifestyle custom of the mother were some of the factors that had individual association with early fetal growth. First-trimester fetal growth restriction is a risk factor that was associated directly with a larger risk in adverse birth outcomes and growth retardation in early childhood period. A broad majority of congenital structural fetal malformations are present as consequence of aneuploidy or any abnormal embryonic development in first 8 weeks of post conception. A series of studies have suggested that other complications of pregnancy such as intrauterine growth restriction, preterm birth and stillbirth also have their origins, at least in part, in early first trimester of pregnancy.

Salomon LJ (2010) [19] - came up with results that at early first trimester majority of the karyotype anomalies and fetal malformations can now be suspected. Any variations seen in early fetal growth can be assessed by different means this could soon help in better identification of the cases that are at risk of abnormal growth i.e. growth restriction as well as macrosomia later in pregnancy.

Papaioannou G, I et al (**2010)**[20] their study was conducted to see the normal Ranges of Embryonic Length, Embryonic Heart Rate, Gestational Sac Diameter and Yolk Sac Diameter at 6–10 Weeks.

Likewise a study was conducted by **Manal El daouk et al (2012)**[21] to see if first trimester crown rump length can predict fetal LGA or SGA; they found that out of 121, Mean first-trimester CRL of the 63 LGA neonates at term was 62.7 ± 6.0 mm, while the other 58 SGA neonates at term was smaller at 58.8 ± 6.9 mm . Thus they concluded that birth weights when taken later on of LGA and SGA term neonates were corresponding to CRL measurements of first trimester, thus, this indicates that the pattern of fetal growth in early pregnancy period is apparent and this continues through term.

Abuelghar et al (2013)[22] demonstrated that viable first trimester pregnancies with smaller Gestational sac and Crown Rump length (CRL) were associated with a higher probability of a subsequent miscarriage. The possibility of early pregnancy loss persists until the end of the

embryonic period- i.e. 70 days after the onset of the last menstrual period. Once a gestational sac was documented on ultrasonographic scanning, subsequent loss of viability in the embryo will occur in 11.5% of pregnancies. After the embryo attains a CRL of 5mm, the probability of subsequent loss falls to 7.2%. The loss rate drops rapidly thereafter to 3.3% for embryos with a CRL of 6mm to 10mm and to 0.5% for embryos with a CRL of 10mm or more(i.e. 5 weeks post ovulation or 7 weeks after Last menstrual period). This is the point where early prenatal investigation can begin.

Harper et al. (2013)[23] have done a study of CRL in dichorionic pregnancies and they observed that dichorionic pregnancies in which CRL discordance was present of approx 11% those are at higher risk for developing fetal anomalies and fetal loss occurring before 20 weeks of gestation. However, they also found that in the absence of any structural anomaly, Crown rump length (CRL) discordance did not appear to be associated with any other adverse outcomes related to continuing pregnancies.

Figueras F, Gratacós E (2014) [24] - Stated the Stage based protocol for managing fetal growth restriction, at every trimester different investigations done invasive as well as non invasive to diagnose if abnormal deviation was seen from the normal curve or adverse outcome. They came up with recommendation of a protocol that facilitate the decisions and it will also reduce the variability in this critical clinical condition. The protocol developed in their study includes evidence based protocol to classify the stages of fetal deterioration and establishes the interval of follow-up and optimal delivery timings.

F D'Antonio el al (2014)[25] came up with the results that Discordance in the fetal dimension is a relatively frequent problem in multiple gestation in pregnancies. The risk of any one fetal demise at 11–14 weeks of gestation was related to the magnitude of CRL discordance at 7+0–9+6 weeks. The correlation between decreased fetal size and fetal loss in pregnancy relies on the fact that discordance in growth could be due to any chromosomal or structural anomaly, which are commonly associated with delayed fetal growth and intrauterine death. On the other hand, growth discrepancy may reflect a state of severe and early placental dysfunction in one

twin , So CRL discordance between 7+0 and 9+6 weeks of gestation is predictive of single fetal loss occurring at a later stage in the first trimester.

Vincent W V Jaddoe et al (2014)[26] studied about the relationship of first trimester fetal growth restriction and any cardiovascular risk factors present in school going children. They came with the result that suggested first trimester of pregnancy is a very important period for the development of further cardiovascular risk component later in life. This observed association is primarily important from an etiological perspective point. Further studies are needed for identification for any underlying causal biological mechanisms and long term consequences. Ways to improve cardiovascular health should start from early pregnancy onwards or even before conception if such threat is detected in time

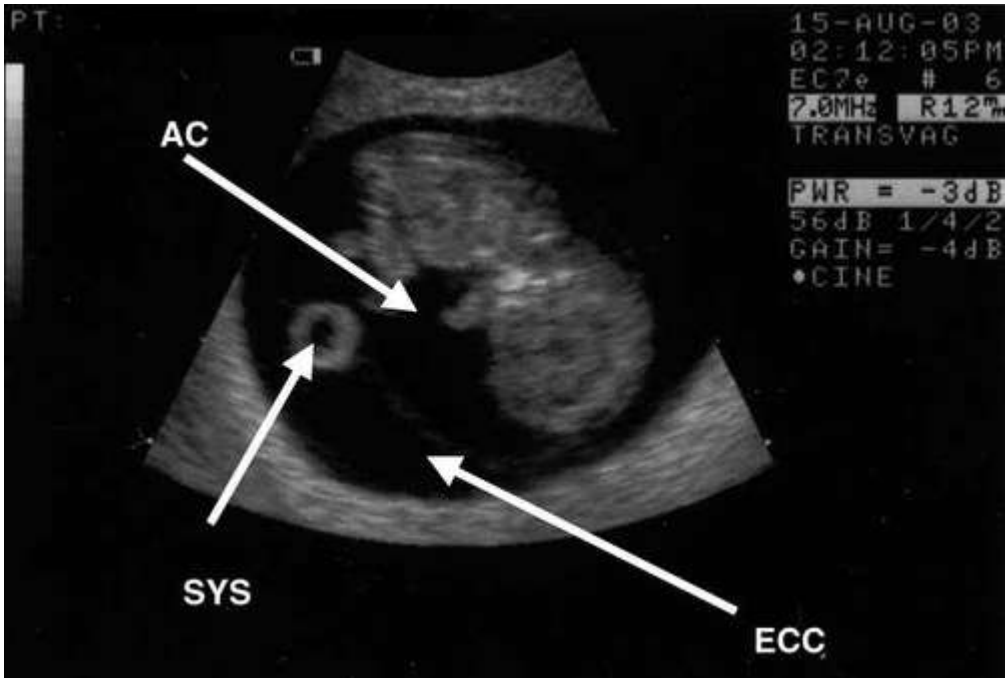

Figure 3 Trans vaginal picture shows a pregnancy of 8-week, demonstrating the exocoelomic cavity (ECC), secondary yolk sac (SYS) and amniotic cavity (AC)

INTERGROWTH-2 PROJECT Papageorghiou AT, Ohuma EO, Altman DG (2014) [6] gave International standards findings and reference for fetal growth based on serial ultrasound measurements.

Nicole Stamatopoulos et al(2015)[27] observed that a woman with advance age faces the problem of clots PV which increases the likelihood of ending up with subsequent miscarriage even if they presented with viable intrauterine pregnancy (IUP) at the primary scan. It was observed in the study that possibility of later pregnancy ending subsequent miscarriage is reduced in women who had presented with a higher fetal heart rate (FHR) in the presence of increased gestational sac (GS) and higher volume/crown-rump length (CRL) ratio.

First-trimester ultrasound measurements are predictor of early abortion. Risk assessment tables based on combinations of abnormal factors are effective in predicting failures and helps in determining timely actions to prevent miscarriage.

Agarwal N et al (2016)[3] study conducted by them gave result that there is a relationship between increasing CRL, Z score finding and risk miscarriage. They found that the possibility of miscarriage increases with any increase in CRL deviation. Adverse environmental exposures lead to developmental adaptations in fetal life.

Dall'Asta, Brunelli V, Prefumo F, Frusca T, Lees CC (2017) [28] – They gave the recommendation of conservative management to focus for the identification of etiology in viable growth restricted fetuses, as prognosis can vary widely in different pregnancies despite of having similar ultrasound findings at the time of diagnose.

Mamta Rath et al(2017)[29]found in their study that crown-rump length (CRL) and fetal heart rate (FHR) below the fifth percentile and FHR below 130 bpm emerged as independent predictors of early spontaneous abortion. Gestational sac dimension (GSD)–crown-rump length (CRL) difference of 12 mm or more and fetal heart rate (FHR) of 128 bpm or less were the optimum cutoff point for continuation of pregnancy. The weakest predictor of

spontaneous abortion was an abnormally sized Yolk Sac diameter in the presence of normal GSD, CRL, and FHR measurements.

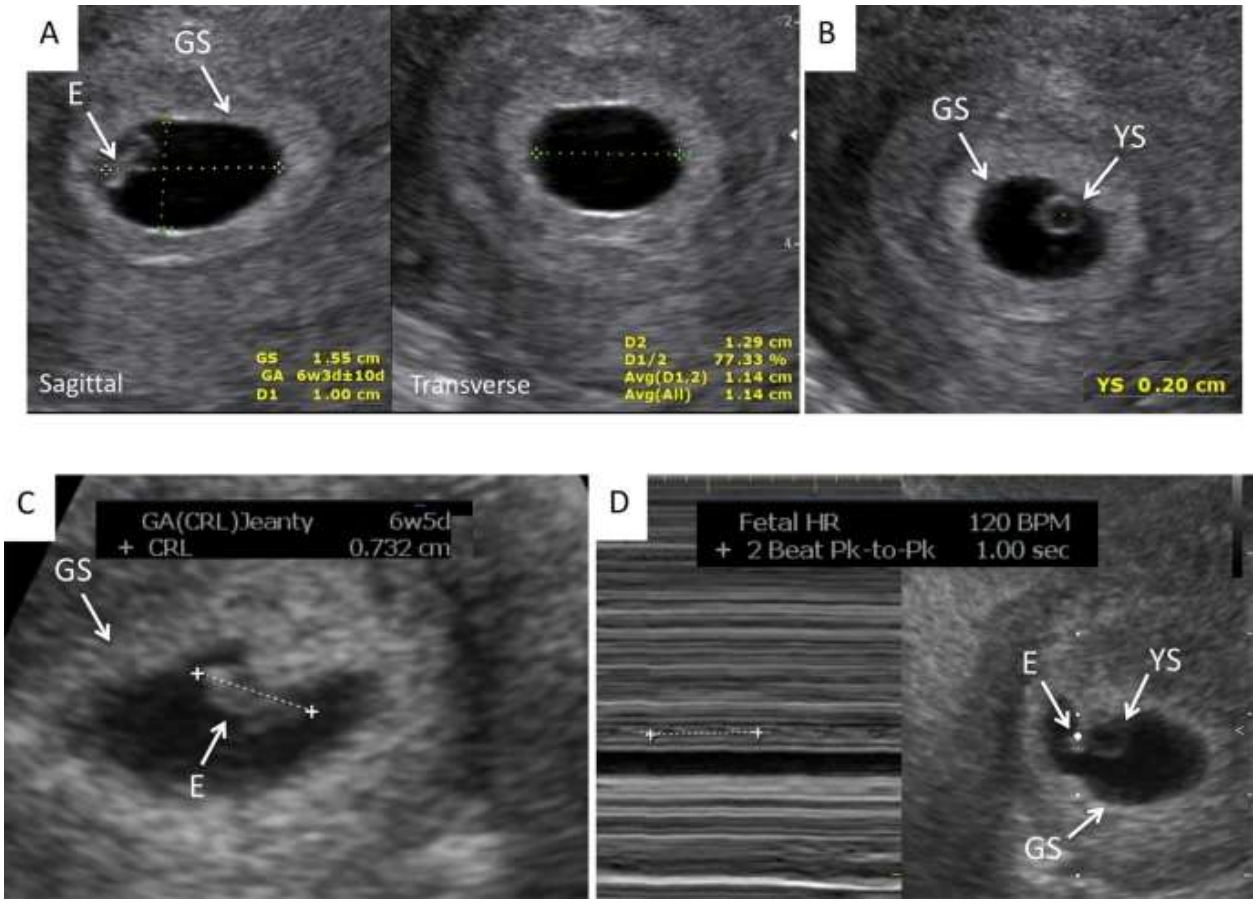

Figure 4

WHO (2017) [5] - Published new multinational fetal growth charts in which it was observed that significant variation is present in fetal growth of different countries. Henceforth WHO is currently working to develop guideline that will allow countries to develop fetal growth charts specific to their own chart accordingly.

Gaccioli F, Aye IL, Sovio U, Charnock-Jones DS, Smith GC (2018) [30] - They studied the fetal growth restriction by screening the fetal biometrical parameters collaborated with maternal serological biomarkers and they concluded that the mechanistic understanding of the

causes of FGR could lead to the development of novel therapeutic approaches, such as repurposing of existing drugs and gene therapy.

Joshua D et al (2018)[30] gave a conclusion that there is strong inverse correlation between gestational sac diameter (mGSD), Crown rump length (CRL) and fetal loss in IVF patients in first-trimester. Although the chances of pregnancy loss with a mGSD − CRL <5 mm was significantly lower than previously reported. They however found that small mGSD − CRL was not associated with an increased risk of complications in pregnancies that continued more than 20 weeks. The association between mGSD, CRL, and miscarriage is complex.

Simic M ,Stephansson O, Petersson G, Cnattingius S, Wikström A (2017) [1] **-** Conducted a study in 69550 pregnancies concluded that Fetal growth below 2.5 [th] percentile during early pregnancy increases further risk of having preterm birth and at term severe fetuses might also be SGA birth irrespective to any disorder associated with the pregnancy.

Ferdos F, Rashid MH, Ma E, Raqib R, Hamada H, Wagatsuma Y (2018) [4] **-** resulted that there is usefulness of assessment of fetal size and growth to identify critical time of fetal growth restriction to improve health status of women of reproductive age in developing countries.

Luthra G, Vuckovic I, Bangdiwala A, Gray H, Redmon JB, Barrett ES, et al (2018) [33] **-** have concluded that Fetal Growth Rate cannot be accurately predicted by using first and second trimester of pregnancy concentration measure of urinary metabolites, such as acetate, formate, tyrosine and trim ethylamine. This highlighted the need of more rigorous investigations and data compilation in the area of early fetal growth restriction as previous studies have been inconsistent after that only after study of metabolites can be theoretically as well as clinically applied to management in obstetrics.

Pillai et al(2018)[34] In the study by they concluded that for prediction of miscarriage individual ultrasound markers like Fetal Heart Rate (FHR), bradycardia in fetus had highest

sensitivity and specificity (sensitivity of 68.41% and specificity of 97.84%) amongst other parameters. They also observed that the sensitivity of FHR is even higher for the pregnant female with threatened miscarriage (sensitivity of 84.18 and specificity of 95.68%). Though, there is gestational age dependent variation seen in fetal heart rate, if fetal heart rate (FHR) is plotted with cut off level versus log diagnostic odds ratio that showed that at ≤110 beat per minute's diagnostic power to predict subsequent miscarriage. Other markers are intrauterine hematoma, crown rump length (CRL) and yolk sac could also predict miscarriage but they found that fetal heart rate (FHR) had higher sensitivity. Therefore in women with a threat of miscarriage and presence of fetal bradycardia on ultrasound scan, ultrasound scan should be repeated in 7 to 10 days to see further prognosis.

Niek Exalto and Eric AP Steegers from the Erasmus Medical Centre, Rotterdam, the Netherlands (2019) [35]

Many studies have been done on the relationship between a small Crown Rump Length and a higher risk of miscarriage or of structural and chromosomal abnormalities that was seen later on in such pregnancies. Measurement of Crown Rump Length (CRL) is a widely accepted method for determining the duration of pregnancy as last menstrual period data have always been subject to recall errors and cannot be relied on. By using sophisticated CRL measurement tools like V-Scope 3D-Virtual Reality which allows very precise calliper positioning, differences were seen between early and late first-trimester embryonic growth corresponding to changes in uterine nourishment from histiotrophic to haemochorial. The study done at Rotterdam periconception cohort (Predict Study) was conducted using above technique demonstrated that periconceptional characteristics also influence embryonic growth. In older mothers the embryo size were larger and also where there was strong consumption to an diet which was energy-rich; embryo was smaller than expected where mothers had history of smoking, alcohol use, troubling cardiovascular risk profile and folic acid supplementation was not taken properly. Robinson et al were probably not aware of such tremendous impact of their scientific work will have on contemporary knowledge of early pregnancy physiology and its pivotal impact on optimizing prenatal care.

Thayer SM, Pilliod RA, Pare E, Vandehey A, Raszka H (2019) [36] - concluded that First trimester prenatal ultrasonography is a great opportunity for identifying fetal structural at the earliest and any growth abnormalities and if early and persistent growth delay is presented with it, practitioners should further consider triploidy as a potential cause for the anomaly. Appropriate counseling should be considered an option for genetic testing must be offered after the discussion of potential risk and benefits to the prospective parents.

Sir Ian Donald (2020)[8] was amongst the first one to demonstrate the application of ultrasound technology to medical diagnosis. Ultrasound waves are the result of an inverse piezoelectric effect. The piezoelectric effect refers to the phenomenon that takes place when pressure is applied to the surface of certain crystals. Inversely, an electric pulse when applied to piezoelectric materials; mechanical pressure produces electric current and that mechanical wave is an ultrasound beam. Many piezoelectric crystals mount together in an ultrasound transducer. After an electric pulse passes it, ultrasound waves are generated, which through the transducer goes into tissue in their path. These waves make a tissue interface, they are reflected back to the transducer and converted to an electric signal, which processes and displays an ultrasound image. Obstetric ultrasound employs a frequency of 1-15 megahertz. Abdominal transducers use a frequency of 1-9 MHz and the transvaginal transducers use frequencies of 5-15 MHz Transvaginal scanning is used in the early first trimester for accurate information regarding early pregnancy complications and fetal morphology. Information may be displayed as a sagittal, coronal, axial or oblique section. There is A mode, B mode and M mode, The B mode studies in motion mode is known as M mode. This is currently employed in obstetrics to evaluate fetal cardiac motion to estimate fetal heart rate and fetal cardiac rhythm as well as to study excursions of cardiac valves and myocardium.

There are some considerations before an ultrasound examination. Patients should be treated with respect, care and reassurance about the painlessness and safety of examination. Prior to changing, the patient must be reminded to empty the bladder prior to transvaginal ultrasound, fasting is not required for transvaginal ultrasound. Transvaginal scans do not require lithotomy position.

Detti L, **Francillon, LChristiansen, M (2020)** [2] – did a prospective cohort study on 252 patients in their study observed that after a gestation period of 5 weeks, a smaller than expected Gestational sac (GS) and a large yolk sac (YS) were reliable markers of pregnancy loss. Early pregnancy ultrasound markers are useful to anticipate a first trimester mislaying.

GS, Yolk Sac, Heart rate and CRL were measured by 2D Transvaginal ultrasound between 6-11 weeks. The YS can reliably identify the event of a miscarriage by observing abnormal yolk sac at minimum of 7 days before its occurrence. Gestational sac (GS) and Yolk sac (YS) are considered to be the earliest parameters that could reliably used as prognostic factors for pregnancy loss, In cases of subsequent miscarriage, they became abnormal as early as 6 weeks of gestation with high sensitivity and specificity. The studies found that of all the assessed parameters in the study, the Yolk sac (YS) were amongst the most reliable single predictor. Crown-rump length (CRL) and embryonic heart rate (HR) became deviated from normal at a later time in pregnancy and were closer to the event, therefore cannot be used for any prognostic application. These findings have important involvement for counseling of patient and planning for care and management, as well as a potential bearing on cost effectiveness within early pregnancy care.

In literature available to anticipate the early miscarriage chance can be done by studying ultrasound findings and also the maternal biochemical markers either alone or in combination. Most common complications occurring in early pregnancy is non viability of pregnancy, intrauterine pregnancy with either an empty gestational sac or a gestational sac accommodating an embryo or fetus with no detectable fetal cardiac activity prior to 12 weeks and 6 days of gestation. This affects roughly 30% of the pregnancies following assisted reproduction and 10% of spontaneously conceived pregnancies. Parameters like Gestational sac (GS), (YS) diameter, crown-rump length (CRL), and embryonic heart rate (HR) are useful in identification of early pregnancy loss. Crown-rump length (CRL) is measured by using an ultrasound during first or early prenatal visit it is generally used in estimation of gestational age in first trimester. It is also executed as a part of regular screening for any abnormality in the number of chromosomes, accompanied by measurements of nuchal translucency (NT) thickness and biochemical markers.

The study of **Devilbiss et al (2020)**[37] was done in early first trimester usage of ultrasound to predict pregnancy loss by characteristics like below than normal fetal heart rate (FHR) and small crown-rump length (≤122, 123, and 158 bpm; ≤6.0, 8.5, and 10.9 mm for gestational weeks 6, 7, and 8, respectively) were observed as independent predictors of assessing clinical pregnancy loss, there was a greater threat observed for pregnancies having both these characteristics The combination of low fetal heart rate (FHR) with a small crown-rump length(CRL) was seen linked to 16% (95% confidence interval, 9.1-23%) risk of subsequent miscarriage, from 5.0% (95% confidence interval, 1.5-8.5%) to 21% (95% confidence interval, 15-27%). Atypical yolk sac diameter or the existence of a sub chorionic hemorrhage did not upgrade the prediction of clinical pregnancy loss.

Yin Xu et al. **(2022)**[38] as per them the maternal characteristic findings were independently correlated with Crown-rump length (CRL) in first trimester of pregnancy, which was negatively related to fetal size, smaller for gestational age (SGA), preterm birth, and admission rate to the NICU, but positively related to larger for gestational age (LGA). These have close relationships with fetal, neonatal, and adult health. For example, researchers have found that there is a risk for SGA babies to develop cerebral palsy, psychological disorders, and poor intellectual performance at term and also in moderate preterm to late preterm infants. For LGA, infants are more exposed to long-term metabolic complications like childhood obesity.

Table 4

Crown Rump length according to weeks

	GA (weeks + days)		
CRL (mm)	50th centile	5th centile	95th centile
5	6+0	5+2	6+5
6	6+2	5+4	7+0
7	6+3	5+6	7+1
8	6+5	6+0	7+2
9	6+6	6+2	7+4
10	7+1	6+3	7+5
11	7+2	6+4	8+0
12	7+3	6+5	8+1
13	7+4	7+0	8+2
14	7+5	7+1	8+3
15	7+6	7+2	8+4
16	8+1	7+3	8+5
17	8+2	7+4	8+6
18	8+3	7+5	9+0
19	8+3	7+6	9+1
20	8+4	8+0	9+2

AJ Praker et al (2022) [39] studied two populations of pregnant women of Asian and Europe countries. These populations were scanned using a linear array real-time ultrasound machines. The crown rump length measurements were made up till 14 weeks of gestational age and till 20 weeks of gestation of pregnancy the biparietal diameter (BPD) is used. Growth curves associated to Crown rump length and biparietal diameter (BPD) measurement to their expected gestational age were plotted on data by the method of unweighted least squares. They observed that between the Asian and European women there was no significant differences in parameters for Crown rump length (CRL) and biparietal diameter (BPD) curves. With aforementioned observation, it was concluded that the European nomograms can be used to estimate Asian fetal gestational age up to 20 weeks.

MATERIAL & METHODS

STUDY DESIGN: Prospective Cohort study

PLACE OF STUDY: Department of Obstetrics & Gynecology, Santosh Medical College Hospital, Ghaziabad, Uttar Pradesh, India

STUDY POPULATION: Women attending the out-patient Department of Obstetrics &Gynecology, Santosh Medical College Hospital, Ghaziabad, with viable singleton intrauterine pregnancies at 5-10 weeks.

DURATION OF STUDY: One year study

INCLUSION CRITERION:

1) Spontaneously conceived pregnancy
2) Viable pregnancy
3) Certain dates (known LMP)
4) Regular menstrual cycles with a cycle length between 26 and 30 days
5) Singleton pregnancy
6) No contraception use in last 6 months
7) No pregnancy or breastfeeding in the 3 months preceding the LMP

EXCLUSION CRITERIA:

1) Doubtful Dates
2) Irregular Cycle
3) Hormonal contraception use within last 6 months
4) Conceived after Assisted reproductive technique
5) Missed abortion
6) Multi fetal pregnancy

METHODOLOGY:

This prospective study was conducted in Santosh Medical College & Hospital, Ghaziabad-201001 (U.P). Clearance was taken from ethical committee of institution. All women attending the outdoor unit with early pregnancy between 5-10 weeks were offered the option of getting included in our study. Those who consented were asked to complete a questionnaire which included demographic features, detailed obstetric & menstrual history and pregnancy symptoms. All women had undergone a TVS using a 5-MHz transducer for B-mode imaging as part of the pregnancy assessment to determine pregnancy location, viability and gestation. In viable pregnancies, the numbers of embryos were documented and measurement of embryonic Crown rump length (CRL) was performed. All women who have viable singleton intrauterine pregnancies and have completed 5–10 weeks of gestation calculated from the last menstrual period (LMP) were included in our study.

Maternal characteristics (demographics, obstetric and menstrual history) and ultrasound findings i.e. CRL, Gestational Sac diameter and FHR were recorded in form of a computerized database at the time of the assessment. All sonographic procedures were done using a TVS (Voluson E6) ultrasound machine equipped with a real time 5-9 MHz endovaginal probe. Pregnancy outcome was then recorded when it was available. The primary outcome was continuing viability of the pregnancy beyond the first trimester, as determined by viability at the routine 11–14 week ultrasound assessment or known viability at a later gestation. To compare the differences in Crown rump length (CRL) between viable pregnancies and those that miscarried subsequently, the deviation of observed and expected CRL was calculated. The observed CRL was calculated from the first ultrasound examinations. The expected Crown rump length (CRL) was calculated based on established growth curves of gestational age and CRL. The difference between the expected and observed CRL was calculated and expressed in SDs (z score).

STATISTICAL ANALYSIS

The presentation of the Categorical variables was done in the form of number and percentage (%) and quantitative data were presented as the mean ± SD and as median with 25th and 75th percentiles (interquartile range). The data normality was checked by using Kolmogorov - Smirnov test. The cases in which the data was not normal, we used non parametric tests. The following statistical tests were applied for the results:

1. The association of the variables which were quantitative and not normally distributed in nature was analyzed using Mann-Whitney Test and variables which were quantitative and normally distributed in nature were analyzed using Independent t test.

2. The association of the variables which were qualitative in nature was analyzed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

3. Receiver operating characteristic curve was used to find out cut off point, sensitivity, specificity, PPV and NPV of observed CRL (mm), expected CRL (mm) and difference in CRL (mm) for predicting missed outcome. DeLong et al test was used for comparison of area under curve of observed CRL (mm), expected CRL (mm) and difference in CRL (mm) for predicting missed outcome.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver. 25.0.

For statistical significance, p value of less than 0.05 was considered statistically significant.

OBSERVATIONS AND RESULT

The study on "**Early first trimester fetal growth restriction and its correlation with adverse pregnancy outcome**" was conducted at Santosh Medical College and Hospital in department of Obstetrics and Gynecology Antenatal Clinic from July 2021 till June 2022 and following observations were made.

Table 5-Incidence of pregnancy outcome

Pregnancy Outcome	Number of cases	Total number of cases	Percentage (%)
Remain Viable	**179**	**215**	**83.26 %**
Subsequent miscarriage	**36**	**215**	**16.74 %**

Over 12 months, 221 women met inclusion criteria. 6 women were lost to follow up. Of the remaining 215, the pregnancy remained viable in 179 (83.26%) and 36 (16.74%) suffered a subsequent miscarriage**. (Table 5, figure 5)**

Figure 5:-Distribution of study subjects according to age

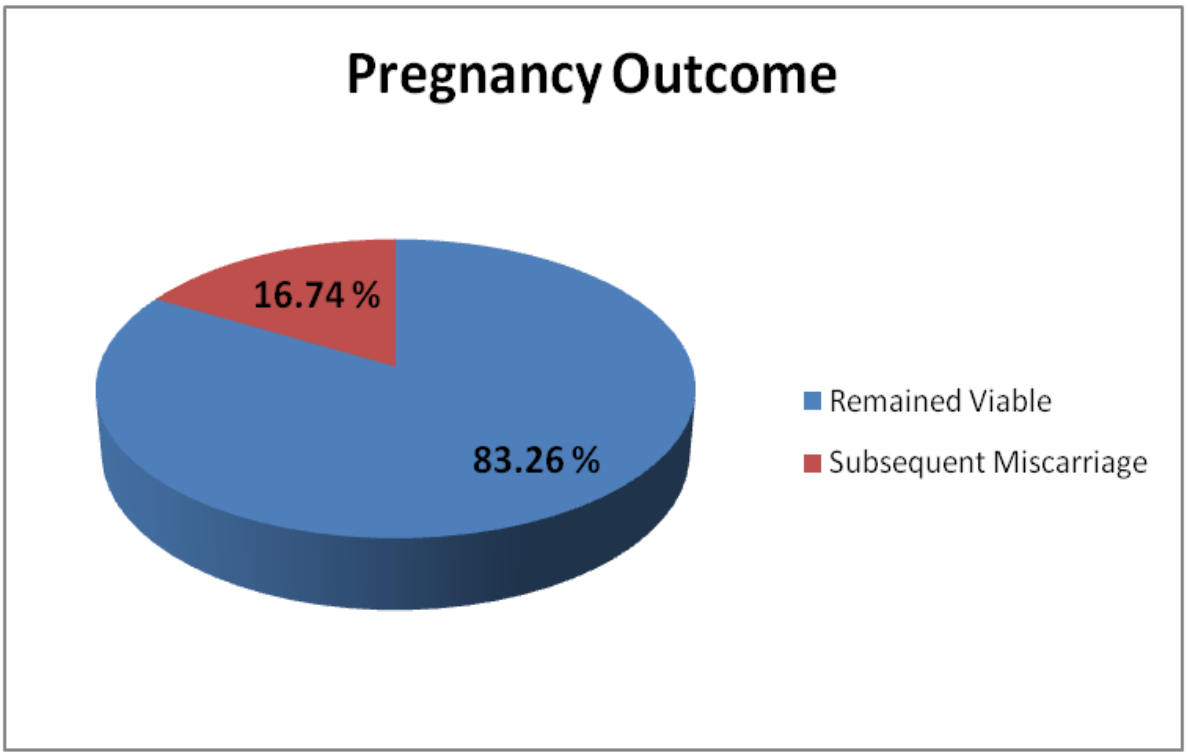

Table: 6 Distribution of study subjects according to age

Age (years)	**Remain Viable** (n_1) = 179		**Subsequent Miscarriage** (n_2) = 36		**Total** Women $n_1 + n_2$ = 215		**P value**
20-25	71	77.2%	21	22.8%	92	42.79%	0.793
26-30	83	88.3%	11	11.7%	94	43.7%	
31-35	19	86.4%	3	13.6%	22	10.2 %	
>35	6	85.7%	1	14.3%	7	3.3 %	
Mean ± SD	25.61 ± 4.26		26.4 ± 4.12		26.27 ± 4.14		
Median(25th-75th percentile)	25(22-27.25)		26(23-28.5)		26(23-28)		
Range	20-36		20-38		20-38		

In our study of 215 patients, 42% patients were in the age group of 20-25 years followed by 43.7% in 26-30 years, 10.2% in 31-35 years and 7% of more than 35 years. Mean ± SD of age (years) in missed outcome was 25.61 ± 4.26 and viable outcome was 26.4 ± 4.12 with no significant association between them, thus, There was no significant correlation between the age distribution and the pregnancy outcome.

Table 6, Figure 6

Figure 6:-Distribution of study subjects according to age

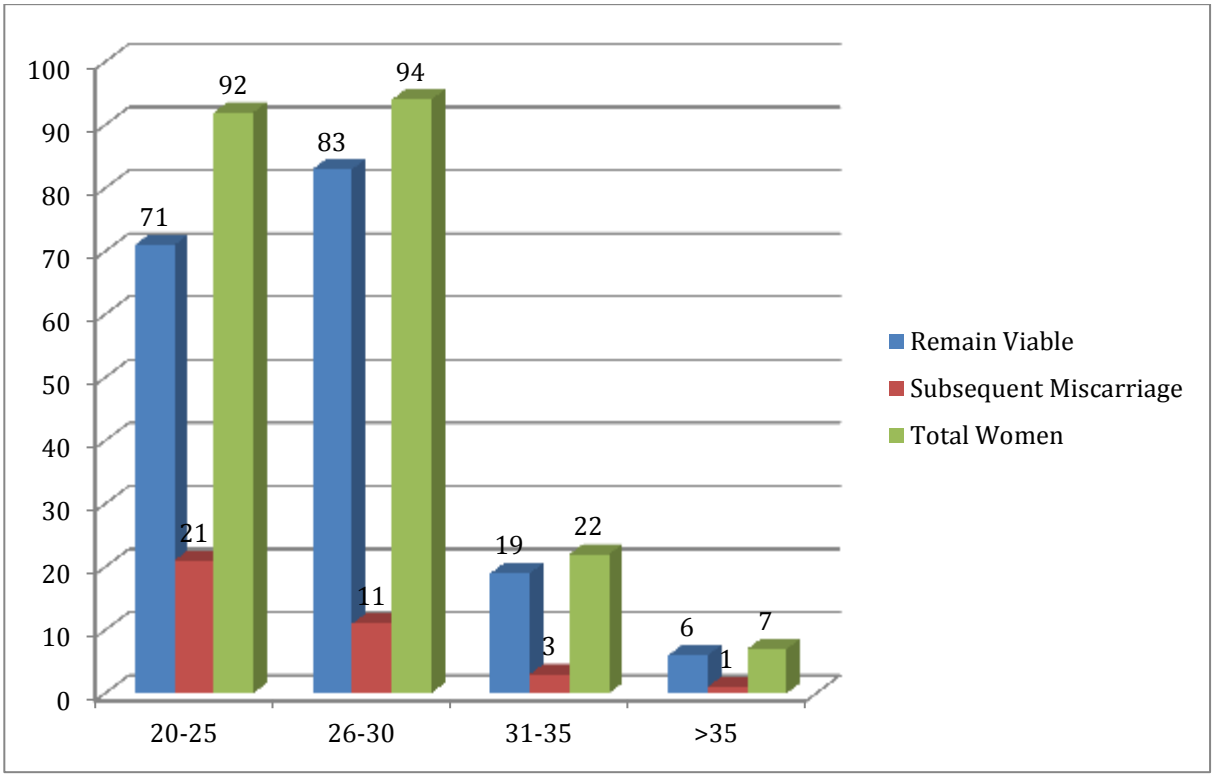

Table 7 Distribution of study subjects according to parity

Parity	Remain Viable $n_1 = 179$		Subsequent Miscarriage $n_2 = 36$		Total Women: $n_1 + n_2 = 215$		P value
0	93	82.30%	20	17.7%	113	52.5%	0.838
1	54	83.08%	11	16.9%	65	30.2%	
>1	32	86.49%	5	13.5%	37	17.2%	

In our study of 215 patients, 113 (52.5%) patients were Primigravida, 65 (30.2%) were second gravida and 37 (17.2%) were multigravida. Out of each category of patients, distributed parity wise, the incidence of patients who had subsequent miscarriage was more or less same.

(**Table 7, figure 7)**

Figure 7:-Distribution of study subjects according to parity

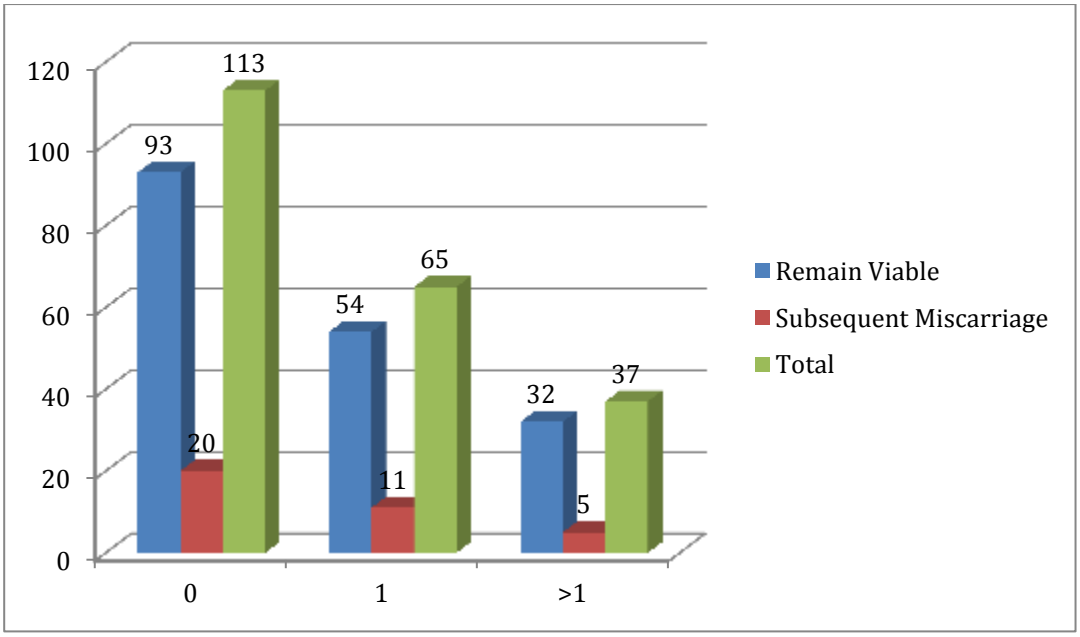

Table 8:-Distribution of study subjects according to religion

Religion	Remain Viable n=179		Subsequent Miscarriage n=36		Total		P value
Hindu	34	17.44%	161	82.56%	195	90.69%	0.539
Muslim	2	10%	18	90%	20	9.30%	
Total	36	16.74%	179	83.26%	215	100%	

In our study of 215 patients, 195 were Hindu, out of these 161 (82.56%) patients continued to have a viable pregnancy and 34 (17.44%) patients had a subsequent miscarriage. Out of 215 patients, 20 were Muslims. Out of those 18 (90%) patients continued to have a viable pregnancy and 2 (10%) patients had a subsequent miscarriage. p value was not significant.

(Table 8, Figure 8)

Figure 8:-Distribution of study subjects according to religion

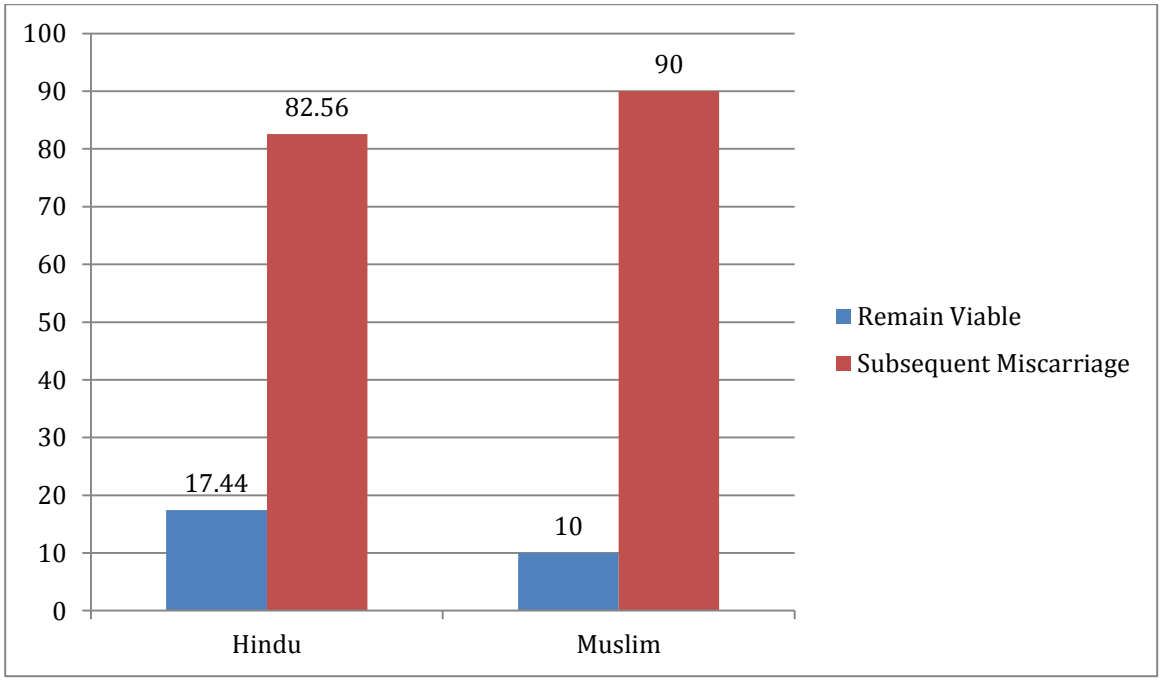

Table 9:-Descriptive statistics of study subjects according to period of gestation

Period of gestation(days)	Remain Viable n=179	Subsequent Miscarriage n=36	Total	P value
Mean ± SD	59.82 ± 6.25	62.25 ± 6.03	60.22 ± 6.26	**0.028**
Median(25th-75th percentile)	59(55-66)	64.5(57.5-67.25)	59(55-66)	
Range	44-70	49-70	44-70	

In our study the mean period of gestation in days was 60.22 ± 6.26 days. The median of period of gestation was 59 days; Range was from 44 to 70. Median (25th-75th percentile) of period of gestation (days) in missed outcome was 64.5 (57.5-67.25) which was significantly higher as compared to viable outcome (59(55-66)). **(p value=0.028)**

(Table 9, Figure 9)

Figure 9:-Descriptive statistics of study subjects according to period of gestation

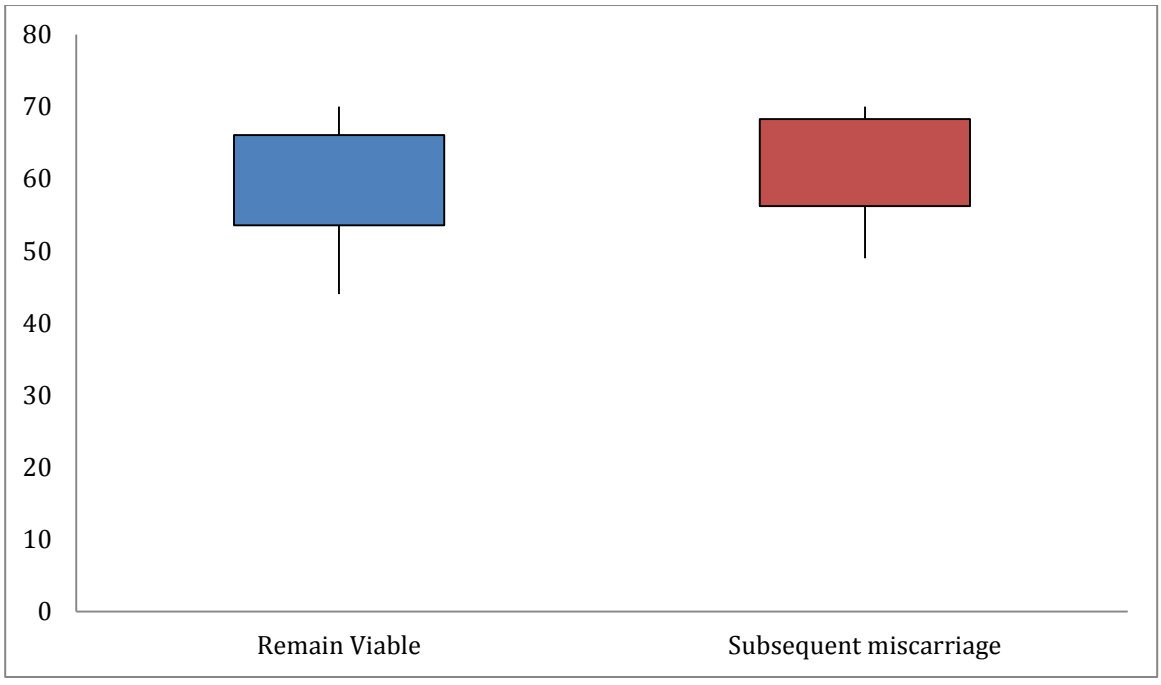

Table 10:-Distribution of study subjects according to complaints

Complaints	Remain Viable n_1 =179		Subsequent Miscarriage n_2=36		Total n_1+n_2	P value
Pain	51	28%	9	25%	60	0.67
Bleeding	20	11%	11	31%	31	**0.003**
Bleeding + pain	10	6%	8	22%	18	**0.001**
Anxiety	62	35%	15	42%	77	0.601
Other	12	7%	1	3%	13	0.7

In our study of 215 patients, patients presented with many symptoms like bleeding or spotting per vaginum, pain in lower abdomen, both bleeding and pain and anxiety besides others. Of the patients that presented with bleeding per vaginum, 11 patients (31%) had subsequent miscarriage as compared 20 patients (11%) that remained viable. (p value=0.003). Of the patients that presented with bleeding + pain, 8 patients (22%) had subsequent miscarriage as compared 10 patients (6%) that remained viable. (p value=0.001). Of the patients that presented with anxiety, 15 patients (42%) had subsequent miscarriage as compared 62 patients (35%) that remained viable. (p value=0.601).

(Table 10, Figure 10)

Figure 10:-Distribution of study subjects according to complaints

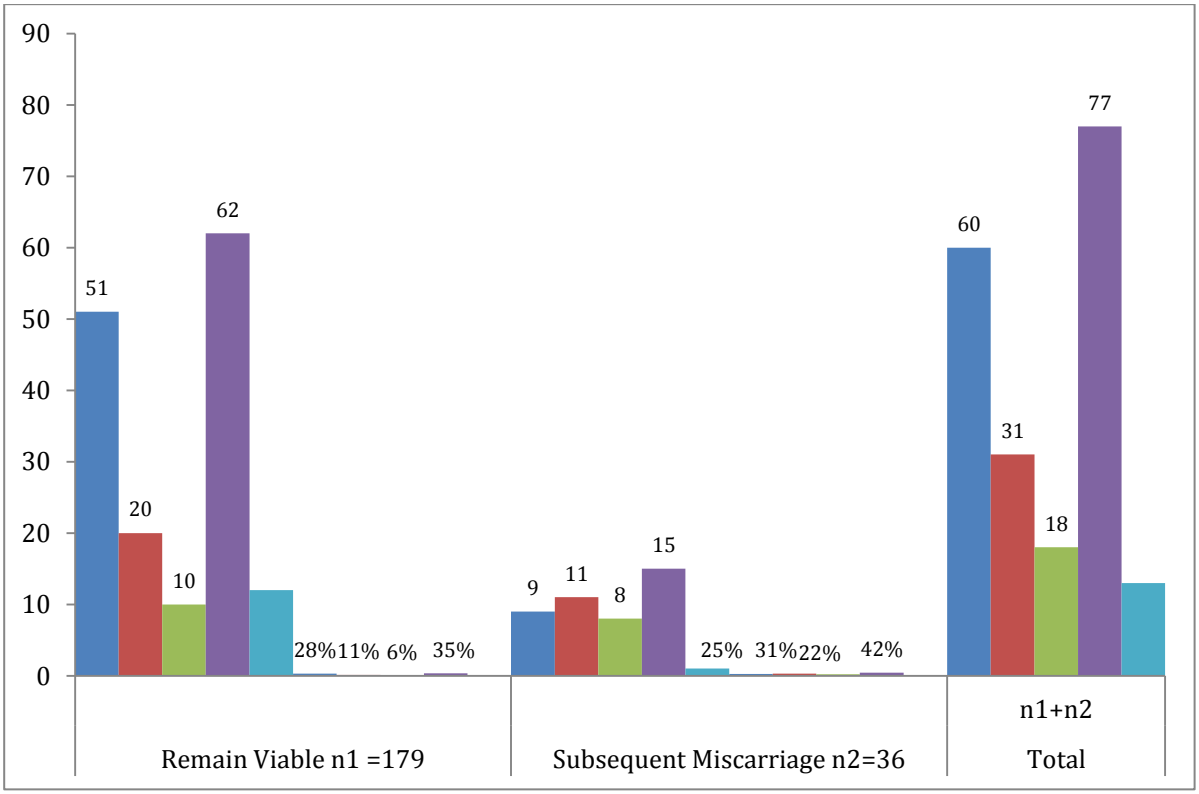

Table 11:-Distribution of study subjects according to previous abortion

Previous miscarriage (Weeks)	Remain Viable n1=179		Subsequent Miscarriage n2		P value
< 12 weeks	44	89.7%	9	9%	1.0
12-24 weeks	5	10.2%	1	1%	
Total	49	27.3%	10	27.7%	

In our study of 215 patients, 179 patients (83.2%) had a viable pregnancy and continued till term. Out of these, 49 patients (27.3%) gave history of one or more miscarriage in previous pregnancies. Of these 44 (83%) had miscarriage of less than 12 weeks and 5 patients (10 %) had miscarriage between 12-24 weeks.

In this study 36 patients (16.7%) has subsequent miscarriage, out of those 10(27.7) patients gave history of one or more miscarriage in previous pregnancies. of those 9 patients (9%) had history of miscarriage before 12 weeks and 1(1%) patient had history of miscarriage between 12-24 weeks.

There was no significant correlation between previous miscarriage and subsequent outcome in present pregnancy.

(Table 11 figure 11)

Figure 11:-Distribution of study subjects according to previous abortion

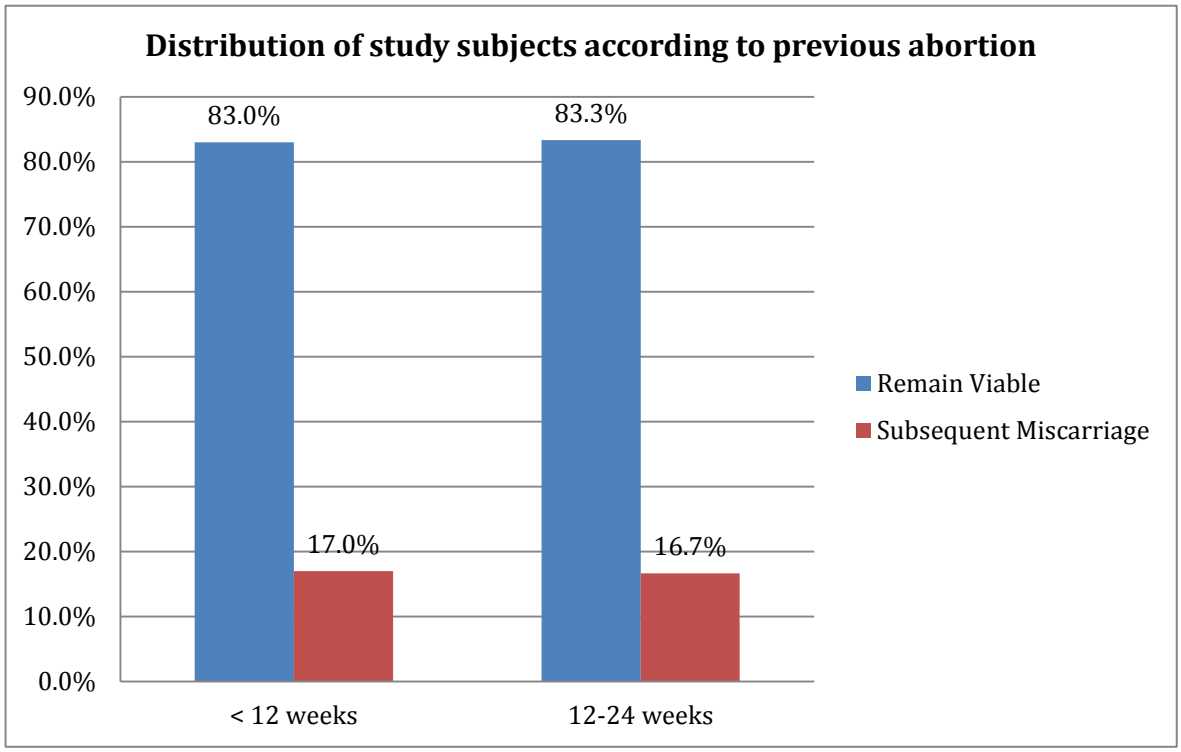

Table 12:-Descriptive statistics of Z score of study subjects

Variable	Mean ± SD	Median(25th-75th percentile)	Range
Z score	-0.98 ± 3.93	-1.57(-2.832--0.522)	-5-33.59

Mean value of Z score of study subjects was -0.98 ± 3.93 with median (25th-75th percentile) of -1.57(-2.832--0.522).

Table 12

Table 13:-Association of deviation of CRL with outcome.

Deviation of CRL	Remain Viable n2 179	Subsequent miscarriage n1 36	Total n1+n2 215	P value
Within 1 SD	77 (100%)	0 (0%)	77 (36%)	<.0001
>1 to 2 SD	45 (91.84%)	4 (8.16%)	49 (23%)	
>2 to 3 SD	36 (75%)	12 (25%)	48 (22.3%)	
>3 to 4 SD	19 (57%)	14 (42%)	33 (15.3%)	
>4 SD	2 (25%)	6 (75%)	8 (4%)	
Total	179 (83.26%)	36 (16.74%)	215 (100%)	

In our study of 215 patients, 36 subsequently landed up in miscarriage. All of these patients had CRL in their first scan less than expected for that gestation. Out of these in 4 patients (8.16%) has their CRL between 1 to 2 SD. 12 patients (25%) had deviation of 2 to 3 SD. 14 patients (42%) had deviation between 3 to 4 SD and 6 patients (75%) had deviation of more than 4 SD.

There were 179 patients, amongst 215 in whom the pregnancy remained viable. In our study 45% (91.84%) patients had CRL less than expected between 1 to 2 SD deviation. 36 (75%) patients had CRL less than expected between 2 to 3 SD. 19 patients (57%) had CRL between 3 to 4 SD. There were 2patients (25%) in whom CRL was lesser than 4 SD nut pregnancy remained viable.

After analyzing the results in viable and subsequent miscarriage groups individually, we also analysed the correlation between the SDs and the percentage of subsequent miscarriage in both the groups jointly.

There were 126 patients out of the study group of 215 ,in whom the SDS was -2 or more. Out of these,122 patients , the pregnancy remained viable. In 4 patients out of 126 patients, there was subsequent miscarriage .This accounted for 3.1% rate of miscarriage (4/126) in the

patients with SDS-2 or more. In 48 patients out of 215 (22.3%),the SD was between -3 to -2 Out of these, in 36 patients (75%), the pregnancy remained viable In 12 patients (25%),there was a subsequent miscarriage .This accounted for 25% rate of miscarriage (12/48) in patients with SDs between -

There were 33 patients out of 215 (15.3%), in whom the SD was between -4 to -3 .Out of these, 19 patients (57%) continued with viable pregnancy; while in 14 patients (42%), there was subsequent miscarriage. This accounted for 42% rate of miscarriage (14\33) in patients with SDs between -4 to -3.

Out of 215,there were 8 such patients (4%), in whom, the SD was -4 or less. Out of these, 2 patients (25%) continued with viable pregnancy; while 6 patients (75%) had a subsequent miscarriage .This accounted for 75% rate of miscarriage (6/8) in patients with SDS -4 or less. Hence, we concluded, that in our study, the rate of percentage of subsequent miscarriage increased with the increase in the deviation of CRL. This rate was only 23% in group with -2 or more SDs; and increased gradually to reach 75% in group with -4 or less SDs.

Proportion of patients with missed outcome was significantly higher in deviation of CRL >2 to 3 SD(28%), >3 to 4 SD(38.71%),>4 SD(25%) as compared to deviation of CRL within 1 SD(0%), >1 to 2 SD(8.16%). (p value <.0001)

Table 13, Figure 12

Figure 12:-Association of deviation of CRL with outcome.

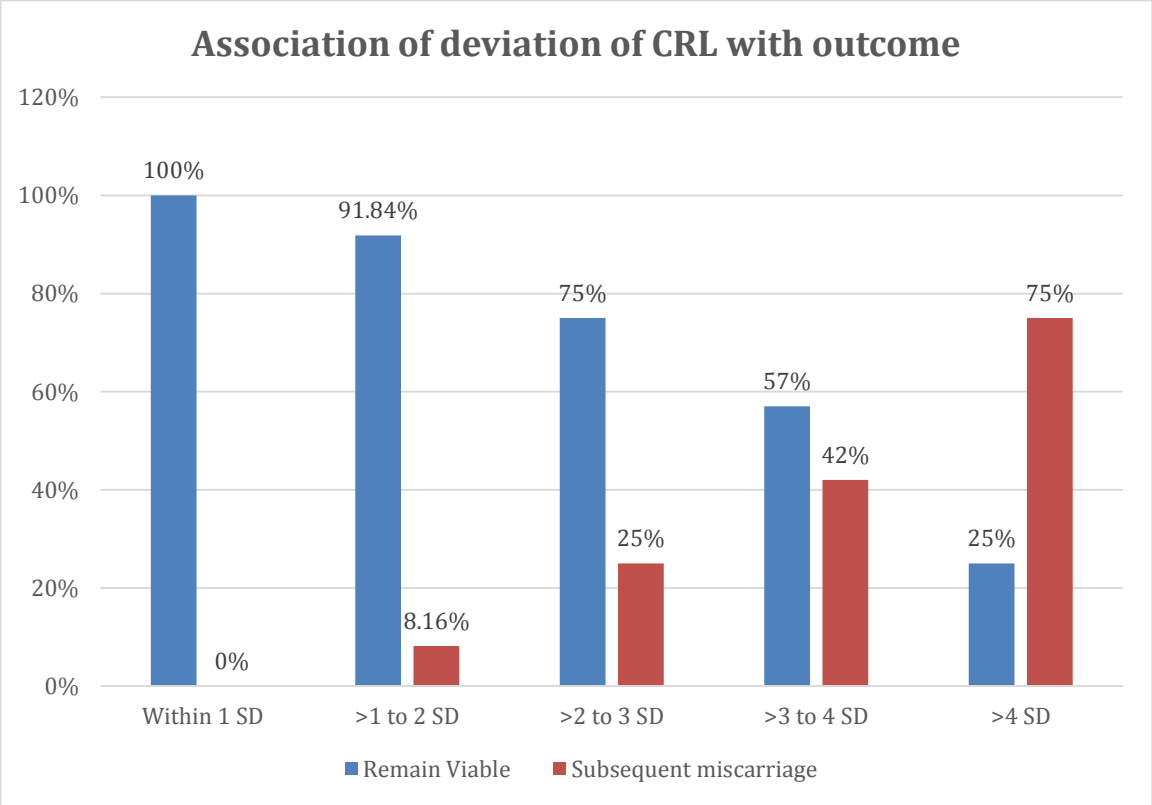

Table 14:-Association of Z score with outcome.

Z score	Missed(n=36)	Viable(n=179)	Total	P value
Mean ± SD	-3 ± 0.89	-0.58 ± 4.18	-0.98 ± 3.93	<.0001
Median(25th-75th percentile)	-2.92(-3.576--2.484)	-1.14(-2.452--0.307)	-1.57(-2.832--0.522)	
Range	-5--1.1	-4.22-33.59	-5-33.59	

The mean z score for CRL in pregnancies that remained viable was-0.58 ± 4.18 and mean z score for missed pregnancy was -3 ± 0.89 , Median(25th-75th percentile) of Z score in viable outcome was -1.14(-2.452--0.307) which was significantly lower in magnitude as compared to missed outcome(-2.92(-3.576--2.484). p value was significant .(p value <.0001).

There was a relationship between increasing CRL deviation, Z score and miscarriage. The risk of miscarriage increased with increasing CRL deviation.

Table 14, Figure 13

Figure 13:-Association of Z score with outcome.(non-parametric variable)

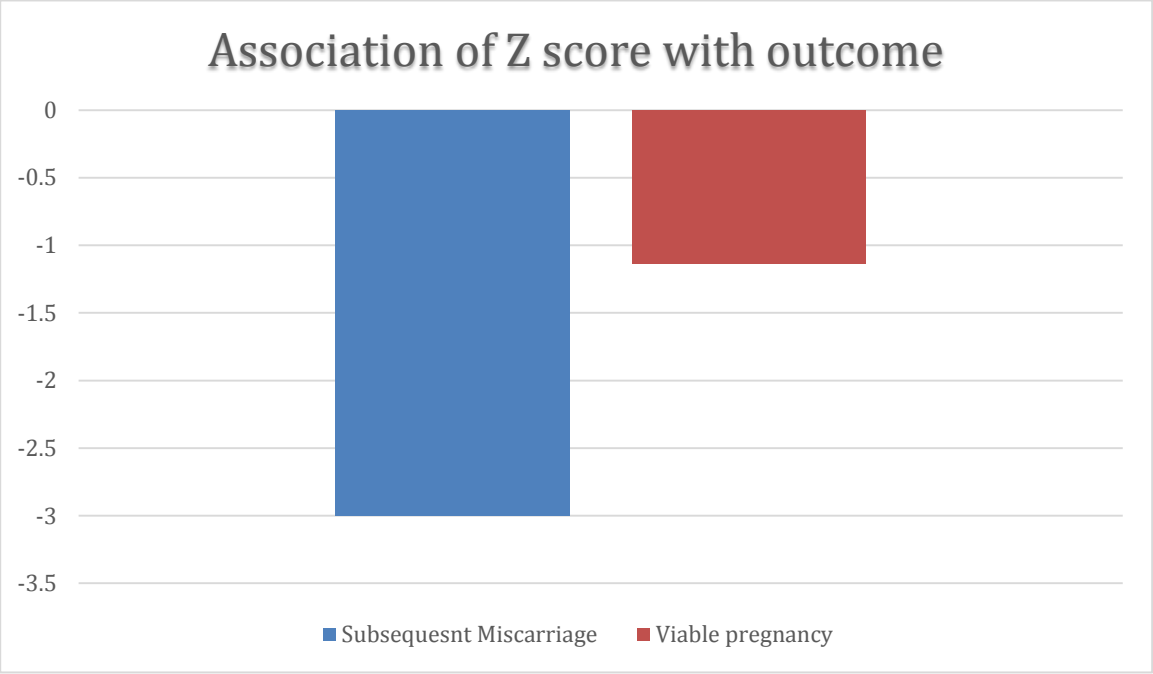

Table 15:-Association of CRL (mm) with outcome.

CRL(mm)	Remained viable (n=36)	Subsequent miscarriage (n=179)	Total	P value
Observed CRL(mm)				
Mean ± SD	19.74 ± 8.39	21 ± 8.03	19.95 ± 8.32	0.411†
Median(25th-75th percentile)	19.74 ± 8.39	23.4(14.3-28.025)	18.4(12.65-26.3)	
Range	5.9-49	7.6-32.6	5.9-49	
Expected CRL(mm)				
Mean ± SD	20.88 ± 6.76	23.78 ± 6.89	21.37 ± 6.85	0.02†
Median(25th-75th percentile)	19.4(15.4-27.5)	26.9(17.9-30.1)	20.5(15.4-27.5)	
Range	6.8-32.8	10.3-32.8	6.8-32.8	
Difference in CRL(mm)				
Mean ± SD	-1.14 ± 3.28	-2.79 ± 2.33	-1.42 ± 3.2	0.0002‡
Median(25th-75th percentile)	-1.2(-2.35--0.35)	-2.4(-3.6--1.375)	-1.4(-2.7--0.4)	
Range	-14.2-21.5	-14.2-21.5	-14.2-21.5	

No significant association was seen in observed CRL (mm) (p value=0.411) with outcome. Mean ± SD of observed CRL (mm) in missed outcome was 21 ± 8.03 and in viable outcome was 19.74 ± 8.39 with no significant association between them.

Significant association was seen in expected CRL (mm) and difference in CRL (mm) with outcome. (p value <.05)

Mean ± SD of expected CRL (mm) in missed outcome was 23.78 ± 6.89 which was significantly higher as compared to viable outcome (20.88 ± 6.76(p value=0.02)).

Table 15, Figure 14

Figure 14:-Association of CRL(mm) with outcome.

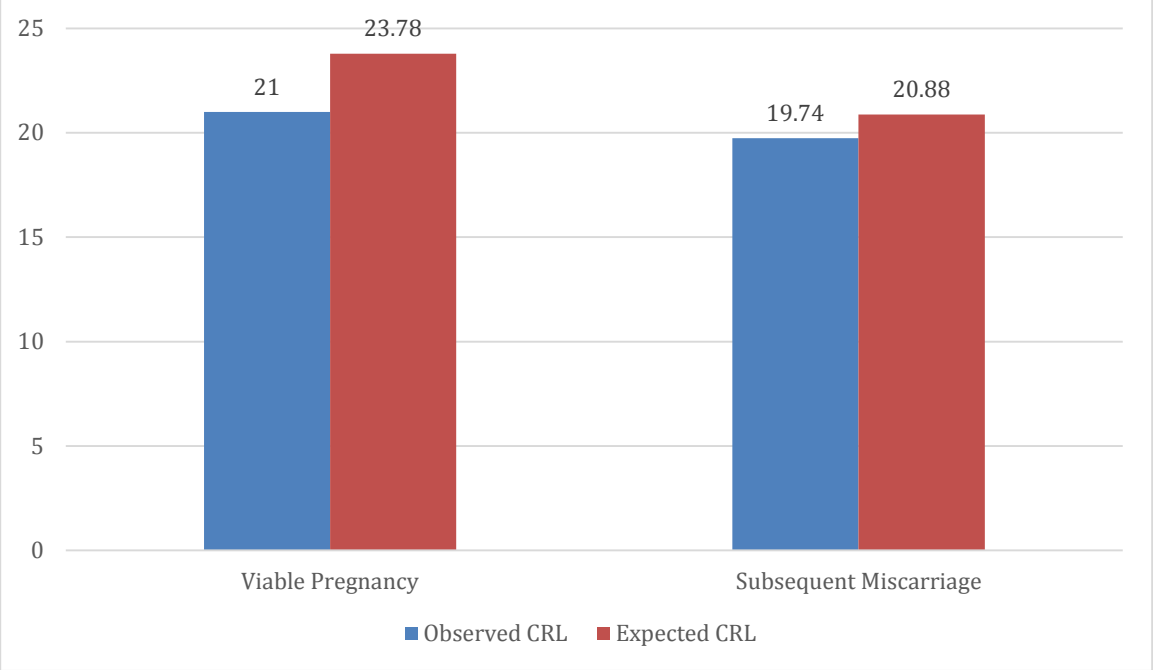

Table 16:- Receiver operating characteristic curve of observed CRL (mm), expected CRL (mm) and difference in CRL (mm) for predicting missed outcome.

Variables	Observed CRL(mm)	Expected CRL(mm)	Difference in CRL(mm)
Area under the ROC curve (AUC)	0.542	0.624	0.698
Standard Error	0.0531	0.0507	0.0438
95% Confidence interval	0.473 to 0.610	0.556 to 0.689	0.632 to 0.759
P value	0.4315	0.0143	<0.0001
Cut off	>24	>25	≤-1.6
Sensitivity(95% CI)	50% (32.9 - 67.1%)	52.78% (35.5 - 69.6%)	69.44% (51.9 - 83.7%)
Specificity(95% CI)	67.04% (59.6 - 73.9%)	70.39% (63.1 - 77.0%)	61.45% (53.9 - 68.6%)
PPV(95% CI)	23.4% (14.5 - 34.4%)	26.4% (16.7 - 38.1%)	26.6% (18.0 - 36.7%)
NPV(95% CI)	87% (80.2 - 92.1%)	88.1% (81.6 - 92.9%)	90.9% (84.3 - 95.4%)
Diagnostic accuracy	64.19%	67.44%	62.79%

ROC curves above the diagonal line are considered to have reasonable discriminating ability to predict missed outcome. Discriminatory power of expected CRL mm) (AUC 0.624; 95% CI: 0.556 to 0.689) and difference in CRL (mm) (AUC 0.698; 95% CI: 0.632 to 0.759) was acceptable. On the other hand, discriminatory power of observed CRL (mm) (AUC 0.542; 95% CI: 0.473 to 0.610) was non-significant. Among all the parameters, difference in CRL (mm) was the best predictor of missed outcome at cut off point of ≤-1.6 (i.e. with the increase in negative difference in CRL, probability of missed outcome increase) with area under curve of 0.698 for correctly predicting missed outcome.

Difference in CRL (mm) had sensitivity of 69.44% followed by expected CRL (mm) (52.78%), observed CRL (mm) (50.00%). On the other hand, expected CRL (mm) had

specificity of 70.39% followed by observed CRL (mm) (67.04%), difference in CRL (mm) (61.45%). Highest positive predictive value was found in difference in CRL (mm) (26.60%) and highest negative predictive value was found in difference in CRL (mm) (90.90%). There is always a trade-off between sensitivity and specificity (any increase in sensitivity will be accompanied by a decrease in specificity) so we choose that variable as best in which combination of sensitivity and specificity gives the maximum predictive value i.e. maximum area under curve so overall difference in CRL(mm) was best predictor of missed outcome.

Table 16 and Figure 15.1 to 15.3.

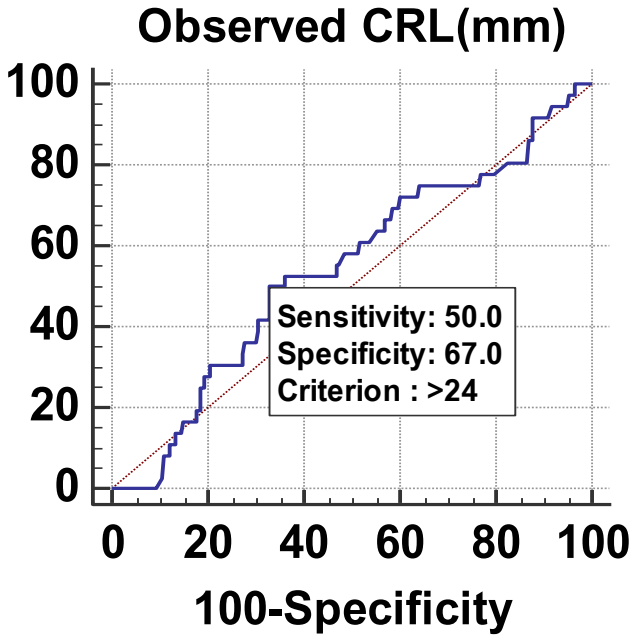

Figure 15.1:-Receiver operating characteristic curve of observed CRL (mm) for predicting missed outcome.

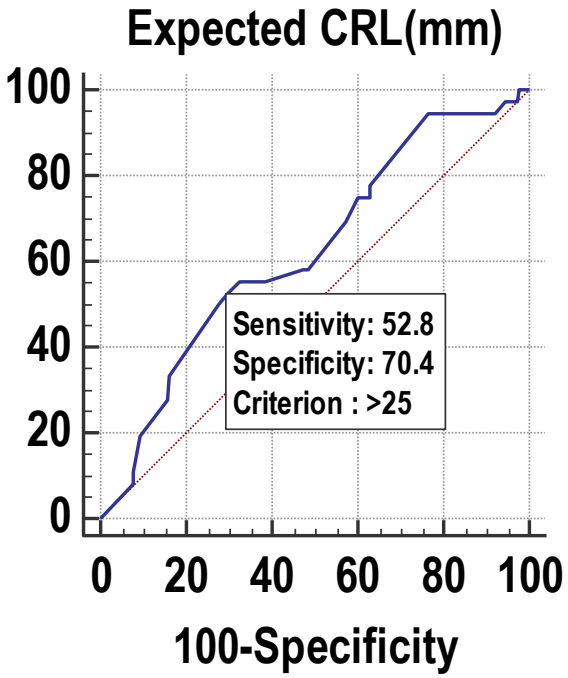

Figure 15.2:-Receiver operating characteristic curve of expected CRL (mm) for predicting missed outcome.

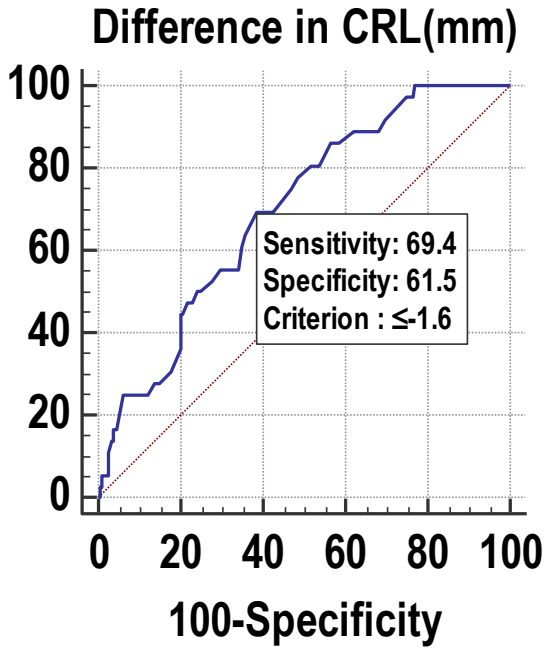

Figure 15.3:-Receiver operating characteristic curve of difference in CRL (mm) for predicting missed outcome.

DISCUSSION

The measurements of embryonic length and heart rate (HR) and those of the gestational sac diameter (GSD) and yolk sac diameter (YSD) have been used for assessment of gestational ge (GA) and prediction of adverse pregnancy outcome, such as miscarriage The measurements of embryonic length and heart rate (HR) and those of the gestational sac diameter (GSD) and yolk sac diameter (YSD) have been used for assessment of gestational age (GA) and prediction of adverse pregnancy outcome, such as miscarriage

Since years, huge efforts has been undertaken to investigate the pathology of growth restricted in fetuses and to enhance antenatal screening. Clinical data has been studied intensively and prospectively, with conflicting risk factors and, in general, poor accuracy is achieved for identifying impairment in fetal growth or morbidity, even when first, second or third trimester ultrasound parameters are added to prediction model. Biomarkers, such as placental growth factor (PlGF), soluble fms - like tyrosine kynase 1 (s-Flt-1) and alpha-fetoprotein, have each been found to show promise as aids to understanding of prognosis of pregnancy. However, Using clinical or ultrasound variables for assessment of gestational age by using measurements such as embryonic length, fetal heart rate, diameter of gestational sac and diameter of yolk sac, a great majority of fetal growth restriction in early pregnancy will be recognized. Either by using population based curves or customised curves. Therefore, there is a real need for better methods of early FGR prediction.

Anne-Marie Nybo Andersen et al[40] in their study they gave result that there was an increasing risk of fetal loss with an increased maternal age in women aged more than 30 years. At more than 40 years, more than half of the pregnancies resulted in adverse outcome. There is an increasing risk observed in both nulliparous women and parous women, regardless of their parity or number of previous spontaneous abortions. Thus, although maternal age was highly related to the parity and reproductive history of the women, their data had shown a strong and independent effect of maternal age as a risk factor. In our study we did not find any significant correlation between increasing maternal age and decreasing CRL (p value 0.793). **AJ Praker et al**[39] have concluded in their study that the European nomograms may be used to

establish Asian fetal gestational age estimation up to 20 weeks. In our study, we used the nomogram curve of CRL for gestation by Robinson and Fleming which has established normal range for early pregnancy biometry. Other studies have also been done to reassess the range given by Robinson and Fleming; in which, the CRL was measured by transabdominal static scanning. Although, our measurements are made by transvaginal sonography, it was previously shown, that, there is no significant difference in the measurements obtained by the two methods (41).

Reem et al[9] had concluded a review on 4510 women in the study they found that painful vaginal bleeding is alarming and had increased risk of bleeding is associated with it, 2% of women in their study had miscarriage. **Hill et al**[42] conducted a review of 347 patients presenting for their obstetric care, and found a statistically significant increase in miscarriage rates in women who had a documented live intrauterine pregnancy and experienced vaginal bleeding versus no vaginal bleeding (12.7% versus 4.2%; P.006). While a study by **Tongsong et** al[43] demonstrated, that, the rate of miscarriage after visualization of fetal heart is higher in women with threatened miscarriage, when compared with a control group without bleeding (5.5 versus 1.9%).While in our study, we also find that women were more likely to have an early miscarriage if they presented with bleeding or bleeding with pain. 31% women (p value 0.003) had complaint of bleeding amongst the women that had subsequent miscarriage and 22% women (p value 0.001) had complaint of bleeding with pain , most of the participants in earlier studies were white, blacks and Hispanics but our study was done on Indian women.

This study, we have demonstrated, that, in women with spontaneously conceived, singleton pregnancies and certain menstrual dates who attended the antenatal clinic, the CRL is below than expected for gestation in all cases that will subsequently end up in miscarriage, ranging from -2 or more SDs to -4 or less SD. Eighty three percent of the continuing pregnancies also had a CRL, which was less than that expected by gestational age, despite women only having been included, if they had certain dates and regular cycles. This circumstance that women might be overestimating gestational age, has been reported before, and, is likely to be attributed to late ovulation or inaccurate reporting of LMP date, although it may be that charts based on apparent LMP, in fact underestimate gestational age. However, in a viable

continuing pregnancy the mean deviation between the observed and expected CRL was -1.14 SD ± 3.28, while it was -2.79 SD ± 2.33 in those pregnancies that subsequently miscarried.

There has been disappointing evidence which may be due to the multifactorial nature of early FGR; the aetiology of the condition is complex and poorly defined. Moreover, placental structure and functioning, maternal and fetal metabolism vary during pregnancy. This is known that at least 70% of first-trimester losses are due to chromosomal abnormalities and, that these can be associated with early growth delay. However, in a study by **Bessho et al**[44] showed that there is at growth delay in foetuses, prior to miscarriage similar finding was seen in both foetuses with normal and abnormal karyotype. Thus, although the reason for the slower rate of fetal growth might be attributable to chromosomal abnormality in the majority, there be another aetiology that affects karyo typically normal fetuses. One possibility is that abnormal placentation could play a role. Histological examination in cases of early pregnancy loss has shown a thinner and more fragmented trophoblastic shell and reduced cytotrophoblast invasion of spiral arteries, than in normal pregnancy; which eventually leads to indirect oxidative stress effects and cellular dysfunction[45]. It is possible, that, embryonic growth could be affected through this process, representing an early manifestation of placental dysfunction. Foetal growth in the first trimester has been studied earlier using single 'one-off measurements of crown-rump length (CRL) or gestational sac (GS) size (**Mantoni and Pedersen**[46] **Falco et al.**[47] **Reljic et al** [48]**Choong et al.**[49] These studies, of women with a pregnancy following in vitro fertilization (IVF) or threatened miscarriage, have shown, that, the observed CRL in pregnancies destined to miscarry is smaller than that expected for gestational age.

In one study, there was an higher chances of miscarriage with an increasing discordance between observed and expected CRL; 13.7% of foetuses with a CRL more than 2SD below that expected for gestational age miscarried compared with an 8.3% miscarriage rate in those with less than 2SD.

Single measurements of small GS size and then a small difference between mean gestation sac diameter (MSD) and CRL have been associated with increased likelihood of miscarriages **Bromley et al.**[50] **Dickey et al.**[51] **Makrydimas et al**[52]

In our study, the possibility of miscarriage after visualisation of a positive foetal heart action was 16%. This is comparable to some studies[51], although, number of other studies have shown lower rates[40]. These differences may be partly explained by the earlier gestational age at presentation in our study. Although, the population in our study was unselected, about half had some vaginal bleeding at the initial presentation.

As **Bell and Loraine, 1965** gave result in their study that there is a normal variation in timing of ovulation, of the order of, plus or minus two days even in patients with regular 28-day menstrual cycles. It therefore follows, that, time interval in which the conception may take place will be at least of four days and possibly be even five days, when the survival time of the ovum in female genital tract, after ovulation, is considered. Secondly, it has been shown that in this investigation, , the inaccuracy in ultrasound measurement of the foetal crown-rump length, is of plus or minus 2 mm. At the 10th week, this is equivalent to plus or minus one day. Finally, the range of the biological variation, which, logically, would be very small in the first few weeks of gestation, would increase as the pregnancy will advance[53].

As in our study, we found that CRL was less than expected in subsequently viable pregnancies (82.3%) and earlier studies have also reported similar findings that many pregnancies with normal outcome are also found to have a CRL or GS size to be less than expected. This is in part due to the fact, that, when using cross-sectional data to assess the fetal size, gestational age assessment relies on accurate recall of the last menstrual period (LMP), **Mukri et al. 2008**[15]. It is known, that, reporting of LMP may cause some bias, with a general tendency for women to overestimate their gestational age (**Savitz et al.**[54]**)** and, thus be found to have a variance between observed fetal measurement and expected fetal measurements.

Furthermore, cycle length may be variable and might get altered by use of any contraceptive hormone. These are the limitations in assessing cross-sectional data mean value, therefore it has been difficult to discriminate between normal and abnormal early pregnancy growth by ultrasound, and, thus difficult to predict women in the general early pregnancy population, who is likely to have an adverse pregnancy outcome.

Our study suggests that despite many women may be overestimating their gestational age but in spite of that smaller-than-expected CRL may also be a sign of early fetal growth delay. We have shown, that, the risk of subsequent miscarriage increases with increasing deviation from the expected CRL.

It is possible that in early pregnancy, growth delay is the consequence of defective development, as it was found by **Dickey et al**[51], Thus, while the risk of miscarriage is 8.16% in those with CRL within 2 SDS, the risk is 25% in patients with SDs between -2 and -3, 42% for patients with SD between -3 and -4 and 75% for patients with less than -4 SDs. It is therefore, reasonable, to offer the mothers further interval ultrasound assessment to confirm the continuation of viability of pregnancy. Whether the policy of re-dating or interval ultrasound is adopted it will be dependent on resource allocation; and policy can be made for arranging follow up of those, in whom the initial ultrasound had shown the largest deviation. Larger longitudinal studies are required to obtain a more detailed orientation for clinical recommendations, regarding counseling of such mothers. Suggestions on when the pregnancy can be reassessed and at what interval the earliest follow up should be done, rather than just simply re-dating. Although, performing such repeated examination in this group of women, it is unlikely to affect the ultimate outcome of the pregnancy, recognition that smaller-than-expected CRL is a marker of early pregnancy failure may aid in the counseling, and it may also reduce the number of women who are found to have unrecognized failed pregnancies at the time of the 11-14 week ultrasound assessment, with its attendant psychological morbidity [55-57].

Early first trimester ultrasound assessment is also useful for accurate dating of pregnancy, early diagnosis of multiple pregnancies, ruling out ectopic pregnancy, measurement of fetal nuchal translucency, detection of major anomalies and the conditions of the uterus and the adnexa and the cervical length. Earliest follow up is should be done for earliest management.

SUMMARY

The present Prospective Cohort study was conducted in department of obstetrics and gynecology, Santosh Medical College, Ghaziabad (U.P) over the period of July 2021 till June 2022. This study was done to evaluate adverse pregnancy outcome in patients with early first trimester fetal growth restriction observed by Ultrasonography.

The aim of this study was to prospectively assess whether the patients with spontaneously conceived, viable singleton pregnancies coming to outpatient antenatal clinic, which subsequently ended in miscarriage exhibit any significantly different pattern of growth from those that remain viable.

All the women who have attended the antenatal clinic were offered the option of being included in this prospective observational study. Only those who agreed were asked to complete a questionnaire including demographic features, detailed obstetric & menstrual histories and pregnancy symptoms. All women underwent a TVS as part of pregnancy assessment to determine location, viability and gestational. In viable pregnancies, the number of embryos were recorded and of embryonic CRL was measured.

All women with spontaneously conceived, viable, singleton intrauterine pregnancies at 5-10 completed weeks of gestation, calculated from the last menstrual period (LMP), with previous regular cycles and with no history of contraceptive use within last 6 months or no breastfeeding within last 3 month of pregnancy, were included.

Patients with doubtful dates, irregular cycles, missed abortions, multiple pregnancy were excluded from this study. Use of any hormonal contraceptives within 6 months or conception through assisted reproductive technique were also excluded.

The primary outcome was observed by continuing viability of pregnancy beyond the first trimester, as determined by viability at routine ultrasound assessment between 11-14 weeks or known viability at a later gestation.

To compare the differences in CRL between viable pregnancies and those that miscarried subsequently, the deviation between observed and expected CRL was calculated. The observed CRL was established from the initial ultrasound examination. The expected CRL was calculated based on established growth curves of gestational age and CRL. These growth curves had been well validated using the transvaginal route. The difference between the observed and expected CRL was calculated and expressed in SDs (z score). Continuous variables between groups, including the z scores were compared Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the prediction of subsequent pregnancy loss following a scan demonstrating a CRL below - 2 SD from the expected mean were calculated. Two-sided P values were reported throughout.

In our study, over 1 year, 221 women met the inclusion criteria. Six (2.7%) women were lost to follow up. Of the remaining 215, the pregnancy remained viable in 179 (83%) and 36 (16.3%) suffered a miscarriage between their initial presentation and the 11-14 week scan. There was no statistically significant difference between age, maternal characteristics, parity or obstetric history between those women who subsequently suffered a miscarriage when compared with women who had continued viable with pregnancy. There was significant difference in the likelihood of miscarriage between those initially presenting with pain alone, bleeding alone, pain and bleeding or neither pain nor bleeding. Patients presenting with bleeding alone(p value 0.003) and bleeding with pain(p value 0.001) were more likely to have subsequent miscarriage. The mean z score for CRL in pregnancies that remained viable was -0.58(SD 4.18), while in those that subsequently miscarried, the mean z score for CRL was significantly larger at -3 (SD 0.89, $P < 0.0001$). In the latter group, the initial CRL was below the expected mean for gestational age in all women.

In pregnancies that remained viable, the observed CRL was corresponding to less than 2SD the expected CRL is 91.84% (45/49) and less than the expected 2SD to 3SD variation CRL in

75% (36/48), the CRL was between 3SD TO 4SD variation is 57% (19/33), the CRL was more than 4 SDs or more below the expected CRL was 25%(2/8). Compared to the subsequent miscarriage the SD more than 4 SD or below was 75% (6/8). The mean z score for CRL in pregnancies that remained viable was-0.58 ± 4.18 and mean z score for missed pregnancy was -3 ± 0.89 , Median(25th-75th percentile) of Z score in viable outcome was -1.14(-2.452--0.307)which was significantly lower in magnitude as compared to missed outcome(-2.92(-3.576--2.484). p value was significant .(p value <.0001).

Thus there is a relationship seen between the CRL, z score and miscarriage, with the risk of miscarriage increasing with the increasing CRL deviation. Using a CRL measurement below 2 SDS and more as a cutoff in predicting difference in CRL yielded a sensitivity of 69.44%, with a specificity of 61.45%, PPV of 26.6% and NPV of 90.9%. As the SD increases there in more risk of subsequent miscarriage observed.

CONCLUSION

The routine usage of TVS in investigating and diagnosing the early Pregnancy problems has led to essential improvements in management of the early pregnancy losses and the patient's perception of the normal and abnormal fetal development in utero.

The ability to make an accurate risk the estimation of the prediction of subsequent pregnancy failure is important not only for the counseling of the individual prospective parents and but also from the broader public health problems in a perspective manner.

This prospective study confirms that in the first trimester growth rate of pregnancies that are destined to subsequently miscarry is significantly lower than those which remain viable. In women with confirmed certain LMP the CRL for that gestation observed was to be smaller in pregnancies that had subsequently ended up in miscarriage as compared to those that had remained viable. All pregnancies that had ended in miscarriage had a CRL below than expected for that gestation, and in seventy five percent of the CRL was at least 4SD or more below expected CRL.

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ANNEXURE I

Ouriginal

Document Information

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Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2021/1830[60] Dated: 17.07.2021

Subject: Grant of Ethical Clearance for Thesis Protocol Topic "**EARLY FIRST TRIMESTER FETAL GROWTH RESTRICTION AND ITS CORRELATION WITH ADVERSE PREGNANCY OUTCOME",** submitted by **Dr. Apoorva Garg,** MD/MS student of Batch 2020-2021, Department of **Obstetrics & Gynaecology**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"EARLY FIRST TRIMESTER FETAL GROWTH RESTRICTION AND ITS CORRELATION WITH ADVERSE PREGNANCY OUTCOME", Dr. Apoorva Garg** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 19.03.2021, 22.03.2021, 24.03.2021, 25.03.2021, 26.03.2021, 27.03.2021 and 06.04.2021. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **12.07.2021** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. V. P. Gupta]
REGISTRAR

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Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Research
4. The Dean – Academics
5. The Director - IQAC
6. Dr Neelima Aggarwal (Guide)
7. HOD of **Obstetrics & Gynaecology**

INFORMED CONSENT

Name of the patient: Age:

Address: Phone Number:

S.NO: Date:

I have been explained the details of the study entitled **"Early first trimester fetal growth restriction and its correlation to adverse pregnancy outcomes"** and my questions regarding the study have been answered to my satisfaction in a language understood by me.

1. I understand that I have the right to withdraw from the study at anytime and to decline to answer any particular question.
2. I understand that my participation in this study is confidential and that no material that could identify me will be used in the analysis and in any reports based on this study.

I hereby provide my consent in the study entitled "Early first trimester fetal growth restriction and its correlation to adverse pregnancy outcomes"

Signature/ thumb impression of the patient

Signature/ thumb impression of witness

सहभागी सुचित सहमति प्रपत्र

गाइडकानाम: -

रोगीकानाम: आयु:

पता: -

फ़ोन नंबर:-

एसएनओ:

मुझे अध्ययन के विवरण समझाया गया है मेरा अध्ययन के बारे में प्रश्नों को एक मेरे द्वारा समझा भाषा में मेरी संतुष्टि का उत्तर दिया गया **"शुरुआती पहली तिमाही में भ्रूण के विकास में वृद्धि और प्रतिकूल गर्भावस्था के परिणामों के साथ इसका संबंध"**

1. मैं समझता हूं कि मुझे किसी भी समय अध्ययन से वापस लेने का अधिकार है और किसी विशेष प्रश्न का उत्तर देने में गिरावट आई है।

2. मैं समझता हूं कि इस अध्ययन में मेरी भागीदारी गोपनीय है और सामग्री जो मुझे पहचान सकती है और रिपोर्ट इस अध्ययन के आधार पर किसी भी में विश्लेषण उपयोग नहीं की जाएगी । मैं इस प्रकार अध्ययन में अपनी सहमति प्रदान करता हूं "शुरुआती पहली तिमाही में भ्रूण के विकास में वृद्धि और प्रतिकूल गर्भावस्था के परिणामों के साथ इसका संबंध "

रोगीकेह स्ताक्षर / अंगूठेकीछाप

गवाहकेहस्ताक्षर / अंगूठेकीछाप

ANNEXURE II

PATIENT INFORMATION SHEET

NAME:
AGE:
ADDRESS:
REGISTRATION NUMBER:
OCCUPATION:
PHONE NUMBER:
CHIEF COMPLAINTS:

PROVISIONAL DIAGNOSIS:

ANNEXURE III

CASE SHEET

Name: Age: Regn. No.

Education Marital status

Husband's Name Occupation

Address

Socio Economic Status

Tel./ Mob. No. Religion

Gravida Parity

Gestational Age (weeks)

LMP EDD

Date of first visit

Date of second visit

CLINICAL DETAILS

Complaints:

Menstrual History:

Obstetrical History:

Allergy History :

Medical/ Surgical History :

FIRST VISIT

PHYSICAL EXAMINATION:

Temp	PR	BP
Pallor	Icterus	Cynosis
Clubbing	Lymphadenopathy	
Edema	Height	Wt
Respiratory System		
CVS		
CNS		
Per Abdomen		
Per Speculum		
Per Vaginum		

INVESTIGATION

Hb	Blood group RH	UPT
USG finding(TVS/TA)		
Period of gestation		
Observed CRL		EXPECTED CRL

SECOND VISIT

Date:

Complaints

Physical Examination:

Temp PR BP

Pallor P/A

P/S

P/V

REPEAT :

Scan done

Period of gestation weeks

Observed CRL

Expected CRL

KEYWORDTOTHE MASTERCHART

AGE – VALUE IN YEARS

RELIGION-

H-HINDU

M-MUSLIM

PARITY-

0 -PRIMIGRAVIDA
1- SECOND GRAVIDA
>1- MULTIGRAVIDA

POG – VALUE IN DAYS

PREVIOUS ABORTION-

LESS THAN 12 WEEKS

BETWEEN 12-24 WEEKS

LOCALITY

U= URBAN

R=RURAL

MASTER CHART

Sno	Locality	AGE	PARITY	RELIGION	POG(days)	PAIN	BLEEDING	BLEEDING+PAIN	ANXIETY	OTHER	PREV.ABORTION	CRL OBS (mm) C	CRL EXP (mm) CI	CRL DIFF	SD	Z SCORE	OUTCOME
1	U	20	0	H	54	no	no	no	no	no	-	12.5	14.5	2	1.34	-1.4925	viable
2	U	20	>1	H	57	no	no	no	no	no	-	16.7	17.4	0.7	1.34	-0.5224	viable
3	R	20	0	H	50	no	no	no	yes	yes	<12wks	10.4	11.1	0.7	1.27	-0.5512	viable
4	R	20	1	H	55	no	no	no	no	no	-	15	15.4	0.4	1.34	-0.2985	viable
5	R	24	0	H	61	yes	yes	yes	yes	no	<12wks	18.4	31.6	13.2	1.13	-11.6814	missed
6	R	20	1	H	70	no	no	no	no	no	-	33	32.8	-0.2	0.14	1.4286	viable
7	R	20	0	H	66	yes	yes	yes	yes	no	<12-24 wks	27.6	27.5	-0.1	0.64	0.1563	viable
8	R	20	1	H	48	yes	no	no	no	no	-	7.2	9.5	2.3	1.14	-2.0175	viable
9	R	20	0	H	53	no	no	no	no	no	-	13	13.6	0.6	1.34	-0.4478	viable
10	R	20	>1	H	53	yes	no	no	no	no	-	10.3	13.6	3.3	1.34	-2.4627	viable
11	R	20	>1	H	59	no	no	yes	no	no	-	19	19.4	0.4	1.2	-0.3333	viable
12	R	20	0	H	55	no	no	no	no	no	-	14.6	15.4	0.8	1.34	-0.5970	viable
13	R	22	1	H	68	yes	no	no	no	no	<12wks	28.7	30.1	1.4	0.35	-4.0000	missed
14	R	20	0	H	70	no	no	no	no	no	-	33.8	32.8	-1	0.14	7.1429	viable
15	R	20	0	H	59	no	no	no	yes	no	<12wks	18	19.4	1.4	1.2	-1.1667	viable
16	R	24	0	H	55	no	no	no	no	no	<12wks	9.2	15.4	6.2	1.34	-4.6269	missed
17	R	20	>1	H	54	no	no	no	yes	no	-	13.8	14.5	0.7	1.34	-0.5224	viable
18	R	21	0	M	59	no	no	yes	no	no		18.4	19.4	1	1.2	-0.8333	viable
19	R	21	>1	H	61	no	no	no	no	no	-	18.8	21.6	2.8	1.13	-2.4779	viable
20	R	21	0	H	66	no	no	yes	no	no	-	25.4	27.5	2.1	0.64	-3.2813	viable
21	R	30	1	H	69	no	yes	yes	yes	yes	<12-24wks	30.9	31.4	0.5	0.28	-1.7857	missed
22	R	21	0	H	54	no	no	no	yes	no		15	14.5	-0.5	1.34	0.3731	viable
23	R	21	0	H	59	no	no	yes	yes	no	-	17.2	19.4	2.2	1.2	-1.8333	viable
24	R	21	0	H	55	yes	no	no	yes	no	-	15	15.4	0.4	1.34	-0.2985	viable
25	R	22	>1	H	53	no	no	no	yes	no	<12wks	13	13.6	0.6	1.34	-0.4478	viable
26	R	22	0	H	70	no	no	no	no	no	<12wks	32.6	32.8	0.2	0.14	-1.4286	missed
27	R	22	>1	H	53	yes	yes	yes	yes	no	<12wks	10	13.6	3.6	1.34	-2.6866	viable
28	R	22	>1	H	70	no	no	no	yes	no	<12wks	33	23.8	-9.2	0.14	65.7143	viable
29	R	22	>1	H	68	yes	no	yes	no	no		30.3	30.1	-0.2	0.35	0.5714	viable
30	R	22	1	H	70	no	no	no	no	no	-	32.9	32.8	-0.1	0.14	0.7143	viable
31	R	22	0	M	59	no	no	no	no	no		7.8	19.4	11.6	1.2	-9.6667	viable
32	R	22	1	H	68	no	no	yes	no	no	-	29.8	30.1	0.3	0.35	-0.8571	viable
33	R	22	0	H	53	yes	no	no	yes	no		10.2	13.6	3.4	1.34	-2.5373	viable
34	R	22	0	H	57	yes	yes	yes	yes	no	<12wks	13.2	17.4	4.2	1.34	-3.1343	viable
35	R	22	1	M	61	no	no	no	yes	no	<12wks	20	21.6	1.6	1.13	-1.4159	viable
36	R	22	>1	H	52	yes	no	no	yes	no	-	12.4	12.7	0.3	1.34	-0.2239	viable
37	R	22	0	H	69	no	no	no	no	no		30.8	31.4	0.6	0.28	-2.1429	viable
38	R	22	0	H	61	no	no	no	no	no	-	20	21.6	1.6	1.13	-1.4159	viable
39	R	22	1	H	65	no	no	no	no	no		25.1	26.3	1.2	0.78	-1.5385	viable
40	R	22	0	H	55	no	no	no	no	no	-	10.4	15.4	5	1.34	-3.7313	viable
41	R	22	1	H	44	no	no	no	no	no	-	5.9	6.8	0.9	0.92	-0.9783	viable
42	R	22	1	H	61	yes	yes	yes	no	no		17	21.6	4.6	1.13	-4.0708	viable
43	R	22	0	M	70	yes	yes	yes	yes	no	<12wks	32.7	32.8	0.1	0.14	-0.7143	viable
44	R	28	>1	H	67	no	no	no	no	no	<12wks	27.8	28.8	1	0.49	-2.0408	missed
45	R	22	0	H	53	no	no	no	no	no		9.2	13.6	4.4	1.34	-3.2836	viable
46	R	23	0	H	58	no	no	no	no	no		29.2	30.1	0.9	0.35	-2.5714	viable
47	R	23	1	H	64	no	no	no	yes	no		25.1	25	-0.1	0.78	0.1282	viable
48	R	25	>1	M	55	no	yes	yes	no	no	<12wks	10.6	15.4	4.8	1.34	-3.5821	missed
49	R	23	0	H	55	no	no	no	no	no	-	13.3	15.4	2.1	1.34	-1.5672	viable
50	R	23	1	H	53	no	no	no	no	no		12.2	12.7	0.5	1.34	-0.3731	viable
51	R	23	>1	H	54	no	no	no	no	no	-	15	14.5	-0.5	1.34	0.3731	viable
52	R	20	0	H	59	no	no	no	no	no	<12wks	14.9	19.4	4.5	1.2	-3.7500	missed
53	R	30	1	H	67	no	no	no	no	no	<12wks	27.2	28.8	1.6	0.49	-3.2653	missed
54	R	25	1	H	59	no	no	no	no	no	<12wks	16.3	19.4	3.1	1.2	-2.5833	missed
55	R	23	1	H	53	no	no	no	no	no	-	12.2	13.6	1.4	1.34	-1.0448	viable
56	R	23	1	H	53	no	no	no	yes	no	<12wks	12.7	13.6	0.9	1.34	-0.6716	viable
57	R	25	0	H	70	no	no	yes	no	no	<12wks	32.4	32.8	0.4	0.14	-2.8571	missed
58	R	35	>1	H	68	no	no	no	no	no	<12wks	29.1	30.1	1	0.35	-2.8571	missed
59	R	22	0	H	68	no	no	no	no	no	<12wks	28.8	30.1	1.3	0.35	-3.7143	missed
60	R	23	1	H	59	no	no	no	yes	no	-	19	19.4	0.4	1.2	-0.3333	viable
61	R	24	0	H	66	no	no	no	no	no	-	26	27.5	1.5	0.64	-2.3438	viable
62	R	24	>1	H	66	no	no	no	no	no	-	26	27.5	1.5	0.64	-2.3438	viable
63	R	24	0	H	66	no	no	no	no	no	-	26.3	27.5	1.2	0.64	-1.8750	viable
64	R	24	1	M	61	no	no	no	no	no	-	22	21.6	-0.4	1.13	0.3540	viable

Sno	Locality	AGE	PARITY	RELIGION	POG(days)	PAIN	BLEEDING	BLEEDING+PAIN	ANXIETY	OTHER	PREV.ABORTION	CRL OBS (mm) C	CRL EXP (mm) CI	CRL DIFF	SD	Z SCORE	OUTCOME
65	R	30	>1	H	66	no	no	no	no	no	<12wks	24.3	27.5	3.2	0.64	-5.0000	missed
66	R	24	0	M	55	no	no	no	yes	no	<12wks	11.3	15.4	4.1	1.34	-3.0597	viable
67	R	24	0	H	53	yes	yes	yes	yes	no	-	8.3	13.6	5.3	1.34	-3.9552	viable
68	R	24	0	H	53	no	no	no	no	no	-	12.1	13.6	1.5	1.34	-1.1194	viable
69	R	22	0	H	69	no	yes	yes	yes	no	<12wks	30.2	31.4	1.2	0.28	-4.2857	missed
70	R	24	0	H	70	no	no	no	yes	no		32.7	32.8	0.1	0.14	-0.7143	viable
71	R	24	0	H	58	no	no	no	no	no	<12wks	15.4	18.4	3	1.27	-2.3622	missed
72	R	24	0	H	59	no	no	no	no	no		16.2	19.4	3.2	1.2	-2.6667	viable
73	R	24	0	H	68	no	no	no	yes	no	-	30.2	30.1	-0.1	0.35	0.2857	viable
74	R	25	0	H	69	no	no	no	yes	no	<12wks	31	31.4	0.4	0.28	-1.4286	viable
75	R	25	0	H	61	no	no	no	no	no	-	19.2	21.6	2.4	1.13	-2.1239	viable
76	R	25	1	H	55	yes	no	no	yes	no	<12wks	12.1	15.4	3.3	1.34	-2.4627	viable
77	R	25	0	H	64	no	no	no	yes	no	-	25.4	25	-0.4	0.78	0.5128	viable
78	R	25	>1	H	53	yes	yes	yes	yes	no	<12wks	12.3	13.6	1.3	1.34	-0.9701	viable
79	R	25	1	H	53	yes	no	no	no	no		12.6	13.6	1	1.34	-0.7463	viable
80	R	25	1	H	52	no	no	no	no	no		8.5	12.7	4.2	1.34	-3.1343	viable
81	R	25	1	H	70	no	no	no	no	no		32.9	32.8	-0.1	0.14	0.7143	viable
82	R	25	1	H	66	yes	no	no	no	no	-	27	27.5	0.5	0.64	-0.7813	viable
83	R	25	0	H	55	yes	no	no	no	no		11.3	15.4	4.1	1.34	-3.0597	viable
84	R	26	1	H	55	no	no	no	yes	no	<12wks	11.2	15.4	4.2	1.34	-3.1343	missed
85	R	28	>1	H	55	no	no	no	no	no	<12wks	10.61	15.4	4.79	1.34	-3.5746	missed
86	R	25	1	H	70	yes	yes	yes	yes	no	<12wks	32.4	32.8	0.4	0.14	-2.8571	viable
87	R	25	>1	H	58	yes	no	no	no	no		15	18.4	3.4	1.27	-2.6772	viable
88	R	25	0	H	63	no	no	no	no	no	-	23	23.9	0.9	0.92	-0.9783	viable
89	R	25	1	H	68	yes	no	no	no	no	-	30.7	30.1	-0.6	0.35	1.7143	viable
90	R	26	1	H	54	no	no	no	yes	no	-	13	14.5	1.5	1.34	-1.1194	viable
91	R	26	0	H	58	no	no	no	no	yes	<12wks	17.6	18.4	0.8	1.27	-0.6299	viable
92	R	26	0	H	68	no	no	no	no	no	-	33	30.1	-2.9	0.35	8.2857	viable
93	R	26	0	H	63	no	no	no	no	no		22.6	23.9	1.3	0.92	-1.4130	viable
94	R	26	1	H	70	no	no	no	no	no	-	33	32.8	-0.2	0.14	1.4286	viable
95	R	26	>1	H	66	no	no	no	no	no	-	49	27.5	-21.5	0.64	33.5938	viable
96	R	26	>1	H	66	no	no	no	no	no	-	28	27.5	-0.5	0.64	0.7813	viable
97	R	35	0	H	59	yes	yes	no	no	no	<12wks	16	19.4	3.4	1.2	-2.8333	missed
98	R	26	0	H	65	no	no	no	no	no		27	26.3	-0.7	0.78	0.8974	viable
99	R	26	0	H	62	no	no	no	yes	yes	<12wks	21.6	22.7	1.1	0.99	-1.1111	viable
100	R	26	0	H	57	no	no	no	yes	yes	-	15.8	17.4	1.6	1.34	-1.1940	viable
101	R	26	>1	H	59	no	no	no	no	no	-	17.1	19.4	2.3	1.2	-1.9167	viable
102	R	22	1	H	52	no	no	no	no	no	<12wks	8	12.7	4.7	1.34	-3.5075	missed
103	R	26	0	H	52	yes	yes	yes	yes	no	<12wks	8.8	12.7	3.9	1.34	-2.9104	viable
104	R	26	0	H	55	no	no	no	yes	no	<12-24wks	14	15.4	1.4	1.34	-1.0448	viable
105	R	26	1	H	70	no	no	no	no	no	-	32.9	32.8	-0.1	0.14	0.7143	viable
106	R	26	0	H	66	no	no	no	no	no		26.3	27.5	1.2	0.64	-1.8750	viable
107	R	26	1	H	63	yes	no	no	no	no		21.2	23.9	2.7	0.92	-2.9348	viable
108	R	26	>1	H	48	no	no	no	no	no		7.3	9.5	2.2	1.13	-1.9469	viable
109	U	26	1	H	59	no	no	no	no	no	-	18	19.4	1.4	1.2	-1.1667	viable
110	U	26	>1	H	66	yes	yes	yes	yes	no	<12wks	26.5	27.5	1	0.64	-1.5625	viable
111	U	26	0	H	58	yes	yes	yes	yes	yes	<12wks	18	18.4	0.4	1.27	-0.3150	viable
112	U	26	>1	H	61	no	no	no	no	no	-	19.3	21.6	2.3	1.13	-2.0354	viable
113	U	26	0	H	66	yes	no	no	yes	no	-	25.4	27.5	2.1	0.64	-3.2813	viable
114	U	26	1	H	60	no	no	no	no	no		18	20.5	2.5	1.2	-2.0833	viable
115	U	26	0	H	68	no	no	no	no	no	-	29.3	30.1	0.8	0.35	-2.2857	viable
116	U	26	0	H	66	no	no	no	no	no		26.1	27.5	1.4	0.64	-2.1875	viable
117	U	26	0	H	53	yes	no	no	no	no	-	12.2	13.6	1.4	1.34	-1.0448	viable
118	U	26	>1	H	65	no	no	no	no	no	-	43	26.3	-16.7	0.78	21.4103	viable
119	U	25	1	H	66	no	no	no	no	no	<12wks	25.2	27.5	2.3	0.64	-3.5938	missed
120	U	26	0	H	68	no	no	no	no	no	-	30	30.1	0.1	0.35	-0.2857	viable
121	U	26	0	H	50	yes	yes	yes	yes	no	<12wks	9	11.1	2.1	1.27	-1.6535	viable
122	U	24	0	H	56	no	no	no	no	no	<12wks	12.2	16.4	4.2	1.34	-3.1343	missed
123	U	26	0	H	55	yes	no	no	yes	no	<12wks	14.6	15.4	0.8	1.34	-0.5970	viable
124	U	24	0	H	61	no	yes	no	no	no	<12wks	18.7	21.6	2.9	1.13	-2.5664	missed
125	U	26	0	H	58	yes	no	no	yes	no	-	17	18.4	1.4	1.27	-1.1024	viable
126	U	26	1	H	58	no	no	no	no	no		16	15.4	-0.6	1.27	0.4724	viable
127	U	27	0	H	51	no	no	no	no	no	-	8	11.9	3.9	1.34	-2.9104	viable
128	U	27	0	H	62	yes	no	no	no	no	-	22	22.7	0.7	0.99	-0.7071	viable
129	U	27	1	H	54	no	no	no	yes	no	-	14.4	14.5	0.1	1.34	-0.0746	viable

Sno	Locality	AGE	PARITY	RELIGION	POG(days)	PAIN	BLEEDING	BLEEDING+PAIN	ANXIETY	OTHER	PREV.ABORTION	CRL OBS (mm) C	CRL EXP (mm) CI	CRL DIFF	SD	Z SCORE	OUTCOME
130	U	23	0	H	49	yes	yes	no	no	no	<12wks	7.6	10.3	2.7	1.27	-2.1260	missed
131	U	27	0	H	48	no	no	no	no	no	-	7.9	9.5	1.6	1.13	-1.4159	viable
132	U	27	1	H	59	no	no	no	no	no		16.4	19.4	3	1.2	-2.5000	viable
133	U	27	1	H	51	no	no	no	no	no	-	7.4	21.6	14.2	1.34	-10.5970	viable
134	U	27	0	H	63	no	no	no	no	no	<12wks	24	23.9	-0.1	0.92	0.1087	viable
135	U	27	1	H	59	no	no	no	no	yes	-	16.2	19.4	3.2	1.2	-2.6667	viable
136	U	27	1	H	70	yes	no	no	no	no	-	32.6	32.8	0.2	0.14	-1.4286	viable
137	U	27	0	H	61	no	no	no	no	no	-	21.3	21.6	0.3	1.13	-0.2655	viable
138	U	27	0	H	61	yes	no	no	yes	no	<12-24wks	19.8	21.6	1.8	1.13	-1.5929	viable
139	U	28	0	H	61	yes	yes	yes	yes	no	<12wks	21	21.6	0.6	1.13	-0.5310	viable
140	U	28	>1	H	55	no	no	no	no	no	-	12.2	15.4	3.2	1.34	-2.3881	viable
141	U	28	>1	H	62	yes	yes	yes	yes	no	<12wks	37	22.7	-14.3	0.99	14.4444	viable
142	U	28	1	H	49	yes	no	no	yes	yes	<12wks	6.8	10.3	3.5	1.27	-2.7559	viable
143	U	36	0	H	70	yes	no	no	no	no	<12wks	32.4	32.8	0.4	0.14	-2.8571	missed
144	U	28	0	M	53	yes	yes	yes	yes	no	<12wks	12	13.6	1.6	1.34	-1.1940	viable
145	U	28	1	H	57	no	no	no	no	no	-	17	17.4	0.4	1.34	-0.2985	viable
146	U	28	0	H	68	no	no	no	no	no	-	32	30.1	-1.9	0.35	5.4286	viable
147	U	28	>1	H	59	no	no	no	yes	no	<12wks	17.1	19.4	2.3	1.2	-1.9167	viable
148	U	28	>1	H	70	no	no	no	no	no		33	32.8	-0.2	0.14	1.4286	viable
149	U	28	>1	H	55	no	no	no	yes	no	<12wks	12.2	15.4	3.2	1.34	-2.3881	viable
150	U	28	0	M	62	yes	no	no	yes	no	<12wks	22.6	22.7	0.1	0.99	-0.1010	viable
151	U	28	0	H	61	no	no	no	no	no		18	21.6	3.6	1.13	-3.1858	viable
152	U	28	0	H	55	no	no	no	no	no	-	14.1	15.4	1.3	1.34	-0.9701	viable
153	U	20	1	H	55	no	no	no	no	no	<12wks	11.2	15.4	4.2	1.34	-3.1343	missed
154	U	28	0	H	54	no	no	no	no	no	-	12.3	14.5	2.2	1.34	-1.6418	viable
155	U	28	1	H	66	yes	no	no	no	no	-	26	27.5	1.5	0.64	-2.3438	viable
156	U	28	0	H	64	no	no	no	no	no		24	25	1	0.78	-1.2821	viable
157	U	28	0	M	61	no	no	no	yes	no	<12wks	19.3	21.6	2.3	1.13	-2.0354	viable
158	U	28	1	H	66	yes	yes	yes	yes	no	<12wks	25.4	27.5	2.1	0.64	-3.2813	viable
159	U	28	1	H	58	no	no	no	yes	no	-	15.3	18.4	3.1	1.27	-2.4409	viable
160	U	28	0	H	66	no	no	no	no	no	-	25.6	27.5	1.9	0.64	-2.9688	viable
161	U	29	0	H	70	no	no	no	yes	no		33	32.8	-0.2	0.14	1.4286	viable
162	U	30	0	H	70	no	no	no	no	yes	-	32.9	32.8	-0.1	0.14	0.7143	viable
163	U	30	0	M	50	yes	no	no	yes	no	<12wks	7	11.1	4.1	1.27	-3.2283	viable
164	U	25	0	H	58	yes	yes	yes	no	no	<12wks	17	18.4	1.4	1.27	-1.1024	missed
165	U	30	0	H	66	no	no	no	no	no		26.1	27.5	1.4	0.64	-2.1875	viable
166	U	30	1	H	66	yes	yes	yes	no	no	-	28	27.5	-0.5	0.64	0.7813	viable
167	U	30	0	M	55	no	no	no	yes	no	<12wks	14.3	15.4	1.1	1.34	-0.8209	viable
168	U	30	0	H	64	yes	no	no	no	no	-	25.3	25	-0.3	0.78	0.3846	viable
169	U	30	1	H	61	no	no	no	no	no	-	21	21.4	0.4	1.13	-0.3540	viable
170	U	27	1	H	66	no	no	no	no	no	<12wks	25.6	27.5	1.9	0.64	-2.9688	missed
171	U	30	>1	H	67	no	no	no	no	no	-	27.3	28.8	1.5	0.49	-3.0612	viable
172	U	30	0	H	64	no	no	no	no	no	-	30	25	-5	0.77	6.4935	viable
173	U	30	0	M	59	no	no	no	no	no		18.6	19.4	0.8	1.2	-0.6667	viable
174	U	30	0	H	55	no	no	no	no	no		11.2	15.4	4.2	1.34	-3.1343	viable
175	U	30	1	M	55	no	no	no	no	no	-	14.7	15.4	0.7	1.34	-0.5224	viable
176	U	30	1	H	53	no	no	no	yes	no	<12wks	8.9	13.6	4.7	1.34	-3.5075	viable
177	U	32	1	H	69	no	yes	yes	yes	no	<12wks	30.6	31.4	0.8	0.28	-2.8571	missed
178	U	30	0	H	53	yes	no	no	no	no	-	12.6	13.6	1	1.34	-0.7463	viable
179	U	30	0	H	59	no	no	no	no	no	-	15.8	19.4	3.6	1.2	-3.0000	viable
180	U	26	0	H	66	no	no	no	no	no	<12wks	25.9	27.5	1.6	0.64	-2.5000	missed
181	U	30	>1	M	55	yes	no	no	no	no	-	12.3	15.4	3.1	1.34	-2.3134	viable
182	U	30	1	H	62	no	no	no	no	no	-	20.2	22.7	2.5	0.99	-2.5253	viable
183	U	30	1	H	55	no	no	no	no	no		12	15.4	3.4	1.34	-2.5373	viable
184	U	30	1	H	68	yes	no	no	no	no	-	29	30.1	1.1	0.35	-3.1429	viable
185	U	31	0	H	53	no	no	no	no	no		12.1	13.6	1.5	1.34	-1.1194	viable
186	U	31	0	H	55	no	no	no	yes	no	<12wks	12.8	15.4	2.6	1.34	-1.9403	viable
187	U	31	1	H	55	no	no	no	yes	no	-	10.5	15.4	4.9	1.34	-3.6567	viable
188	U	27	0	H	64	no	no	no	no	no	<12wks	22.5	25	2.5	0.78	-3.2051	missed
189	U	31	>1	H	53	no	no	no	no	no		11	13.6	2.6	1.34	-1.9403	viable
190	U	32	0	M	70	no	no	no	no	no	-	36	32.8	-3.2	1.14	2.8070	viable
191	U	32	0	H	54	no	no	no	yes	no	<12wks	12.4	14.5	2.1	1.34	-1.5672	viable
192	U	32	0	M	54	no	no	no	no	no	<12-24wks	12.6	14.5	1.9	1.34	-1.4179	viable
193	U	32	1	H	66	no	no	no	no	no	<12wks	26.3	27.5	1.2	0.64	-1.8750	viable
194	R	32	1	H	66	no	no	no	no	no	-	25.1	27.5	2.4	0.64	-3.7500	viable

Sno	Locality	AGE	PARITY	RELIGION	POG(days)	PAIN	BLEEDING	BLEEDING+PAIN	ANXIETY	OTHER	PREV.ABORTION	CRL OBS (mm) C	CRL EXP (mm) CI	CRL DIFF	SD	Z SCORE	OUTCOME
195	R	32	1	H	59	no	no	no	no	no		16.4	19.4	3	1.2	-2.5000	viable
196	R	32	>1	H	69	no	no	no	no	no	-	32.6	31.4	-1.2	0.28	4.2857	viable
197	R	26	0	M	66	yes	no	no	no	no	<12wks	24.6	27.5	2.9	0.64	-4.5313	missed
198	R	32	1	M	59	yes	no	no	no	yes	<12-24wks	15.4	19.4	4	1.2	-3.3333	viable
199	R	33	0	H	55	yes	yes	yes	yes	yes	<12wks	14.9	15.4	0.5	1.34	-0.3731	viable
200	R	33	0	M	66	yes	no	no	yes	no	<12wks	24.8	27.5	2.7	0.64	-4.2188	viable
201	R	33	>1	H	53	no	no	no	yes	yes	<12wks	13	13.6	0.6	1.34	-0.4478	viable
202	R	34	1	H	68	no	no	no	no	no	-	30.5	30.1	-0.4	0.35	1.1429	viable
203	R	34	0	H	50	yes	no	no	yes	no	<12wks	9	11.1	2.1	1.27	-1.6535	viable
204	R	21	0	H	65	no	no	no	no	no	<12wks	24.4	26.3	1.9	0.78	-2.4359	missed
205	R	35	0	H	55	no	no	no	no	no	-	14.2	15.4	1.2	1.34	-0.8955	viable
206	R	35	1	H	66	yes	yes	yes	yes	yes		26.3	27.5	1.2	0.64	-1.8750	viable
207	R	20	0	H	55	yes	yes	yes	no	no	<12wks	12.5	15.4	2.9	1.34	-2.1642	missed
208	R	27	0	H	59	no	no	no	no	no	<12wks	17.6	19.4	1.8	1.2	-1.5000	missed
209	R	36	0	H	61	no	yes	no	yes	no	-	18.4	21.6	3.2	1.13	-2.8319	viable
210	R	36	1	H	63	no	no	no	yes	no	<12wks	23.6	22.7	-0.9	0.99	0.9091	viable
211	R	37	0	H	61	no	no	no	no	no	-	21	21.6	0.6	1.13	-0.5310	viable
212	R	37	0	H	55	no	no	no	no	no		14.6	15.4	0.8	1.34	-0.5970	viable
213	R	20	1	H	66	yes	yes	no	no	no	<12wks	25.3	27.5	2.2	0.64	-3.4375	missed
214	R	38	0	H	57	yes	no	no	yes	no	<12wks	13.6	17.4	3.8	1.34	-2.8358	viable
215	R	38	>1	H	61	no	no	no	yes	no	<12wks	21.8	21.6	-0.2	1.13	0.1770	viable